IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. a Massachusetts Corporation Plaintiff, v. Arthrex, Inc., a Delaware Corporation, *et al.* Defendants.	)	Civil Action No. 04-12457 PBS

DEFENDANTS ARTHREX, INC.'S AND PEARSALLS, LTD.'S REPLY MEMORANDUM IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT

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I. INTRODUCTION

DePuy Mitek's Opposition to Defendants' Motion for Summary Judgment ("DePuy Mitek Opp."), like its previous submissions, continues to take simple, straightforward issues and tries to sow confusion in the hope that the Court will be misled into believing that there are factual issues where none exists.

Wherever possible, DePuy Mitek runs away from its own patent. It has to, because any rational review of the '446 patent leaves no question that it has nothing to do with FiberWire. Simply put, the '446 patent teaches a braid where the first set of yarns (of which "PE" is one of the identified materials) is a highly pliable, lubricious material which is used to improve the pliability and handleability of the braid, but needs to be combined with a second "strength" yarn because the pliable, lubricious material is too weak to be used alone. Unlike the "first yarn" of the '446 patent, UHMWPE (the alleged first yarn) is very strong and stiff, the exact opposite of what is described in the '446 patent. Unable to dispute these indisputable facts, DePuy Mitek instead creates an Alice in Wonderland world in which a "strong" material can still be "weak" and in which a stiff material can still be pliable. That is the length to which DePuy Mitek goes in its desperate attempt to create the illusion of a factual dispute.

There is no more straightforward issue in this case than the claim construction question of whether "PE," as that term is used in the '446 patent, includes UHMWPE. DePuy Mitek says that it does; defendants say no. Yet, in an argument that shows the lengths to which DePuy Mitek will go try to create confusion, DePuy Mitek makes the incredible argument that even if the Court adopts *defendants'* interpretation, there still is a factual issue as to whether UHMWPE literally is "PE." Obviously, that cannot be so.

But that is just a precursor of what is to come. DePuy Mitek spends page after page arguing that even if the Court agrees that UHMWPE is not included within the interpretation of

"PE," there still is a factual dispute over whether UHMWPE is equivalent to the materials identified in the first set of yarns. But if the Court rules in favor of defendants on the "PE" claim construction issue, it is because the Court agrees that the '446 patent teaches that the first group of yarns are materials that are highly pliable materials, but too weak to use alone as sutures. UHMWPE is strong and stiff -- exactly the opposite. How can a material that is so different be substantially the same? The answer to that simple question is equally as simple: It cannot be, and no amount of spin can create a factual dispute.[1]

DePuy Mitek's response fares no better when it gets to the "consisting essentially of" issue. DePuy Mitek begins by telling the Court that defendants' summary judgment motion on this issue is predicated solely on the Court agreeing with defendants' interpretation of the basic and novel characteristics of the claimed invention (DePuy Mitek Opp. at 1), when it knows that defendants contend that they are entitled to summary judgment under both defendants' and DePuy Mitek's interpretation. This cannot be an oversight because DePuy Mitek later presents argumentation, albeit without any evidence, that defendants are not entitled to summary judgment under DePuy Mitek's interpretation of the basic and novel characteristics. DePuy Mitek Opp. at 19.

DePuy Mitek's discussion of the merits on the coating issue ignores the overwhelming evidence that universally shows that coating affects handleability (particularly knot tie down)

[1] What DePuy Mitek asserts are factual issues precluding summary judgment, *e.g.*, what is "general purpose PE", "what is the function of the claimed first fiber-forming materials", "what are the "basic and novel properties of the claimed sutures" (DePuy Mitek Mem. at 1), are the same issues involved in the Court's claim interpretation determination. DePuy Mitek cannot magically convert legal issues for the Court into factual issues by raising the same arguments under the guise of an infringement analysis. *See, e.g., Phonometrics, Inc. v. Northern Telecom, Inc. et al*, 133 F.3d. 1459, 1464 (Fed. Cir. 1998) (stating "disputes concerning the meaning of claims do not preclude summary judgment, because the resolution of those disputes is part of the process of claim interpretation, a question of law").

and presents absolutely *no* evidence that FiberWire is somehow an exception to this rule. It cannot present any such evidence because no such evidence exists.

DePuy Mitek's response to defendants' argument that the '575 patent invalidates the claims of the '446 patent tries to create factual issues by grossly misrepresenting defendants' position. DePuy Mitek has to do so because it does not and cannot dispute defendants' explanation of the disclosure of the '575 patent or the admissions of its own expert. DePuy Mitek's effort to create a factual dispute should be seen for what it is -- an irrelevant sideshow that should be ignored.

Likewise, there is nothing to DePuy Mitek's effort to create a dispute of fact as to whether the '575 patent is prior art. As defendants' showed in their Opening Memorandum ("Def. S.J. Mem."), the '575 patent is prior art because Ethicon did not reduce its invention to practice before the filing date of the '575 patent. DePuy Mitek never disputes the legal proposition that it is a requirement that the embodiment built *must* include *every* limitation of the claim, nor does it dispute the fact that the braids actually built by Ethicon were not sterilized, a limitation of every asserted claim of the '446 patent. That should be the end of the matter.

II. DEFENDANTS ARE ENTITLED TO SUMMARY JUDGMENT IF THE COURT CONSTRUES "PE" AS DEFENDANTS REQUEST

A. Literal Infringement

Incredibly, DePuy Mitek contends that even if the Court adopts defendants' proposed claim interpretation of "PE," defendants are not entitled to summary judgment of no literal infringement because there is a factual issue of whether UHMWPE constitutes general purpose PE. DePuy Mitek Opp. at 5. DePuy Mitek can make this argument only by willfully ignoring defendants' claim interpretation brief, defendants' answers to interrogatories and every thing else that has occurred in this case over the past two years. Indisputably, defendants' proposed interpretation of "PE" to mean "general purpose PE" is predicated on a finding that general

purpose PE *excludes* UHMWPE because the '446 patent's description of "PE" is diametrically opposed to UHMWPE. *See, e.g.*, Defendants' Opening Brief on Claim Construction at 10-16. Should the Court agree with defendants' proposed interpretation, obviously there is no dispute that UHMWPE does not literally fall within the meaning of PE. DePuy Mitek's inability, or unwillingness, to recognize the obvious cannot change this result.

B. There Are No *Genuine* Issues Of Material Fact Regarding The Doctrine Of Equivalents

DePuy Mitek spends 10 pages of its Opposition desperately trying to create a factual dispute of whether UHMWPE is "equivalent" to the first set of yarns from the group consisting of PTFE, FEP, PFA, PVDF, PETFE, PP and PE. But everything that DePuy Mitek argues ignores these basic facts: (1) UHMWPE is incredibly strong and stiff and (2) defendants' claim construction of "PE" is based on the teachings of the '446 patent that the first set of yarns are weak and pliable, the opposite of UHMWPE. Should the Court agree with defendants' claim construction of "PE," as we believe it will, then the only possible conclusion is that the undisputed facts demonstrate that the differences between the first set of yarns and UHMWPE are quite substantial and there can be no infringement under the doctrine of equivalents.

Unable to dispute these indisputable facts, DePuy Mitek embarks on a series of irrelevant or misguided arguments designed to create the illusion of a factual dispute. DePuy Mitek contends that Dr. Brookstein presented "two different and consistent analyses" (an insubstantial differences test and function/way/result test) under the doctrine of equivalents (DePuy Mitek Opp. at 6) in an effort to have this Court believe that there are two methods to prove infringement under the doctrine of equivalents. That is not correct. In *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 24 (1997), the Court explained that there is only one test for infringement under the doctrine of equivalents – the insubstantial differences test. The Court

did say that in appropriate cases, the function/way/result test can be used to show that the differences are insubstantial, but it remains a single test. *Id.* at 39-40.

Dr. Brookstein's original Expert Report did not present two analyses, but rather *only* contended that the function/way/result test shows infringement under the doctrine of equivalents. Ex. 1 at ¶¶ 53-66.[2] As we showed in our opening brief, Dr. Brookstein's function (and result) analysis – that "the function of the first set is to contribute a property that is different from the second set" is hopelessly flawed. Def S.J. Mem. at 11-12. Dr. Brookstein admitted that under his analysis *any* material would meet his functional identity as long as it contributed anything to the suture different from the second yarn. *Id.* at 12. In its Opposition, *DePuy Mitek never attempts to defend this fatal flaw or otherwise disagree with defendants' assertions*.

DePuy Mitek argues that Dr. Brookstein based his function/way/result analysis on the claims, citing to three bullet points. DePuy Mitek Opp. at 9. The first two bullet points speak generally to the function of "dissimilar fiber-forming materials." While Dr. Brookstein did rely on those two bullet points in his report, those aspects of the specification have nothing to do with the *issued claims* of the '446 patent. As explained in defendants' Opening Memorandum, the application as originally filed contained broad claims requiring only that two dissimilar materials be braided together. But those broad claims, to which the first two bullet point relate, were *abandoned* during prosecution (a fact that DePuy Mitek does not dispute). DePuy Mitek's assertion that Dr. Brookstein relied on the third bullet point, which does relate to the function of the specifically-identified polymers of the claims, is simply untrue. Dr. Brookstein *never referenced this portion of the specification in his function analysis.* Ex. 1 at ¶¶ 54-56.

[2] Dr. Brookstein, in his Rebuttal Report, did provide opinions, albeit flawed and without basis, disagreeing with Dr. Muhkerjee, who opined that the differences between UHMWPE and the first set of yarns were not insubstantial.

Accordingly, the undisputed facts are that Dr. Brookstein's analysis is not based of the *actual, issued* claims of the patent.

Unable to dispute the real facts, DePuy Mitek repeats its oft-stated refrain that the functions identified by defendants are only for "'preferred embodiments,' not for the claims as a whole." DePuy Mitek Opp. at 10. Apparently, DePuy Mitek believes that if it repeats this argument enough times it will become true. The simple and undeniable facts are that the broad claims were abandoned, and that *all* of the claims identify the first set of yarns as one of the seven specifically-listed polymers. Thus, what DePuy Mitek continually calls "preferred embodiments" are nothing more than the claims themselves.[3]

Dr. Brookstein's "insubstantial differences" analysis, even if it could be considered a second analysis, presents nothing that raises a *genuine* issue of material fact. Importantly and dispositively, DePuy Mitek never disagrees with the undisputed fact that the '446 patent states that the first set of yarns are pliable and are included to increase braid pliability. Dr. Brookstein also never disagrees that UHMWPE is stiff and that, in FiberWire, PET (the material from the second set of yarns), *not* UHMWPE, is included to increase pliability. Likewise, DePuy Mitek has no answer to the undisputed fact that UHMWPE is added to FiberWire for improved strength (Def. S. J. Mem. at 11), while the '446 patent ascribes that function to the second set of yarns, *not* the first set. DePuy Mitek's inability to address these dispositive differences is the death knell to its "insubstantial differences" argument.

[3] DePuy Mitek makes a curious argument, accusing Arthrex of picking only one function of the first set of yarns and ignoring the other "alternative" functions. DePuy Mitek Opp. at 10. DePuy Mitek never explains the relevancy of its argument and we know of none. In addition, with regard to the bullet point to which DePuy Mitek refers, the various functions are not in the alternative, but instead are connected by the word "and." Accordingly, even if DePuy Mitek's twisted logic were correct, it would mean that UHMWPE would have to perform *all* the listed functions to be equivalent. Even DePuy Mitek makes no such assertion.

The little bit that DePuy Mitek does say is both irrelevant to the insubstantial differences test and is unsupported by any evidence. DePuy Mitek makes a convoluted argument that there is equivalence because PET was added to the FiberWire braid to provide what Dr. Brookstein calls "knot holding strength." DePuy Mitek Opp. at 7. This argument is irrelevant because the equivalency argument is between UHMWPE and the first set of yarns; it has nothing to do with PET and the second set of yarns.

In any event, DePuy Mitek's argument about the role of PET has no support in the record. Relying on Dr. Brookstein, DePuy Mitek claims that "PET imparts strength (namely at least knot holding strength) to the heterogeneous braid" (DePuy Mitek Opp. at 7), and that Mr. Grafton confirms this fact. But when Dr. Brookstein described the function of PET in his Expert Report, however, he only asserted that PET's function is to provide flexibility. There is not a word about strength. Ex. 1 at ¶ 56. Moreover, Dr. Brookstein simply makes up the word "knot holding strength" to describe what is the well-known property of knot security. While DePuy Mitek blithely asserts that "[k]not holding strength is a recognized suture strength property," its sole support for that statement is Dr. Brookstein's declaration where he *cited absolutely nothing* for this made up term. Ex. 2 at ¶ 20. DePuy Mitek also mischaracterizes Mr. Grafton's testimony. While Mr. Grafton explained, over and over again, that a purpose of adding PET was to improve the knot security of the braid (Ex. 3 at 53:8-19, 53:24-54:5), he was not testifying that PET was added to improve the strength of the braid. In fact, he said the exact opposite. Mr. Grafton testified that the strength of the braid, without PET, was excellent. Ex. 3 at 45:16-46:9.

But even if there were some merit to DePuy Mitek's attempt to twist knot security into a "strength" criteria (and there is none), it has nothing to do with strength, as that term is used in the '446 patent to describe the attributes of the second set of yarns. Without question, that

description is speaking of tensile strength of the materials, going so far as to describe the specific amount of yarn tenacity that is desired. Ex. 4 at col. 4, ll. 36-39.

The patent could not be clearer that "strength" is a word used to describe the tensile properties, that is "straight and knot tensile strength." Ex. 4 at col. 6, ll. 32-36; Table at col. 7-8, using "strength" to describe tensile and knot strength. When describing the different property of knot security, the patent does *not* use the word strength (Ex. 4 at col. 6, ll. 36-44), a fact that Dr. Brookstein was reluctantly forced to admit. Ex. 5 at 373:2-15. This is but one example of DePuy Mitek's "Alice in Wonderland" approach to claim construction. Make up the word "strength" to describe something else, and then wrongly argue that its made up term is what the patent describes as "strength" when all the evidence is to the contrary.[4]

DePuy Mitek throws in an almost incomprehensible argument that "Arthrex's Counsel's Nonequivalency Arguments Are An Insufficent Basis For Granting Summary Judgment In The Face Of Expert Testimony." DePuy Mitek Opp. at 10-12. While this argument is difficult to follow, two things are clear. First, it is predicated on DePuy Mitek's game of, when all else fails, blame the lawyers for making up arguments. DePuy Mitek's unseemly accusations have no basis in reality. Defendants' attorneys never make up a thing. Every argument presented is based on the evidence in the case, usually on the '446 patent,[5] a document that DePuy Mitek tries to minimize, unless it is forced to comment in response to defendants' reliance on that intrinsic evidence.

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[4] For these same reasons, DePuy Mitek's effort to describe UHMWPE as "weak" (DePuy Mitek Opp. at 12, n.9) is wholly without merit. The simple and undeniable fact is that UHMWPE is strong, the opposite of weak.

[5] To make DePuy Mitek's accusation even more scurrilous, in this instance, the interpretations proffered by defendants is supported by its expert, Dr. Mukherjee. Ex. 6 at 23-25. Defendants chose not to include those materials in its original presentation because the Federal Circuit has instructed us that experts' opinions on the meaning of the patent is disfavored evidence, but rather, the determination should be made by examining the patent disclosure itself. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318-19 (Fed. Cir. 2005) (en banc). DePuy Mitek either does not understand, or chooses to ignore, the Federal Circuit's instructions.

Second, DePuy Mitek cannot present strained arguments over the proper interpretation of the patent and then assert that factual disputes have been created. DePuy Mitek's arguments relate to the proper construction of the patent, issues that are matters of law for the Court to determine. *Markman v. Westview Instruments, Inc*., 517 U.S. 370, 372 (1996). DePuy Mitek cannot, with the wave of its hand, convert these legal issues into a factual conflict by presenting them under the rubric of infringement. *See, e.g., Phonometrics,* 133 F.3d. at 1464.

In any event, as defendants' best understand the arguments, DePuy Mitek seems to be contending that the '446 patent did not really mean that the pliable, lubricious substances are weak even though the patent describes them as "relatively weak and unusable." DePuy Mitek Opp. at 11, citing to '446 patent at col. 2, ll. 22-25. If there were *any* merit to DePuy Mitek's strained interpretation, and there is absolutely none, why would the very next sentence of the patent teach that there is a tradeoff between braid strength and pliability? Ex. 4 at col. 2, ll. 26-28. Why would the patent, when speaking about the very lubricious yarns identified in the claims, teach that these materials need to be combined with second yarns "which act to provide improved strength to the heterogeneous braid?" *Id.* at col. 4, ll.9-40. Why does the patent state that too high a percentage of "lubricating yarns" may "adversely affect the overall strength of the braid?" *Id.* at col. 4. ll. 52-54. And why do the only tests that Ethicon chooses to report show that the lubricating yarns tested were weak? *Id.* col. 7, ll. 25-34 and Table. There is, of course, only one answer. The teachings of the '446 patent could not be clearer -- the lubricating yarns from the first set of yarns are too weak and must be combined with a stronger yarn.[6]

Finally, DePuy Mitek presents another confusing argument apparently intending to create the impression that there is a factual dispute over whether UHMWPE was added to FiberWire to

[6] DePuy Mitek's contention that defendants' assertions are undercut because PP also "is available in an ultra high molecular weight form" (DePuy Mitek Opp. at 11) has nothing to do with the teachings of the patent and thus, even if accurate (we note that its "evidence" says nothing about the existence of this product in 1992 when the patent was filed), is irrelevant.

improve pliability. DePuy Mitek Opp. at 12-14. It is surprising that DePuy Mitek would make such an argument because its expert originally opined that UHMWPE was included for strength and PET was added for "flexibility." Ex. 1 at ¶ 56; Ex. 5 at 296:18-297:10. Moreover, DePuy Mitek's new argument simply makes no sense. The highlight of DePuy Mitek's argument is its astonishing contention that a material that it acknowledges is too stiff can somehow still contribute to pliability. DePuy Mitek Opp. at 12-13. The same material cannot be both pliable and stiff at the same time, the two are polar opposites, as the '446 patent itself teaches. Ex. 4 at col. 8, ll. 41-42 ("[b]ending rigidity is the inverse of pliability"). DePuy Mitek may live in a make believe world where "stiff" doesn't mean "stiff," just like "weak" doesn't mean "weak," but it cannot create a factual dispute in the real world where this case must be decided.

III. DEFENDANTS ARE ENTITLED TO SUMMARY JUDGMENT BECAUSE COATING AFFECTS THE BASIC AND NOVEL CHARACTERISTICS OF THE CLAIMED INVENTION

On the coating issue, DePuy Mitek's Opposition does not even try to dispute defendants' overwhelming evidence that coating affects handleability features of sutures, especially knot tie down. DePuy Mitek does not dispute that this fact is so universally known that it is included in multiple patents, including many Ethicon patents, in its own expert's patent, in Ethicon publications and is supported by the testimony of every relevant witness in this case. Def. S. J. Mem. at 14-15. DePuy Mitek's inability to question these unassailable facts should be the dispositive answer to this issue.

In a nutshell, DePuy Mitek's argument appears to be that, despite these universally-known facts, FiberWire, somehow, is the only suture ever created where coating does not affect handleability characteristics. It has no evidence to support any such notion. DePuy Mitek did

not perform any tests of the effect that coating has on any suture characteristics, or at least any such tests that it produced to defendants.[7]

Instead, DePuy Mitek asserts that defendants did not produce evidence that coating affects FiberWire handling properties. First, the accusation is simply not true. As DePuy Mitek well knows, defendants did produce evidence that the coating on FiberWire improves the handleability characteristics of "knot sliding, knot tying and ease of passing suture through tissue." See Def. S. J. Mem. at 15.[8] Since DePuy Mitek cannot respond to the evidence (because it knows that it is true), it tries to be cute, telling this Court that the document does not "support an argument that the coating materially affects *the pliability of the suture*." DePuy Mitek Opp. at 18 (emphasis added). At the same time, however, DePuy Mitek tells the Court that "it does *not* address *[coating's] affect on pliability*" and that it is *only* addressing "the evidence of whether the coating materially affects handleability." DePuy Mitek Opp. at 15 (emphasis added.) This is just another example of DePuy Mitek's incapability of playing it straight with this Court.

Second, DePuy Mitek's argument is irrelevant. Since this is an infringement issue, the burden is on DePuy Mitek to come forward with affirmative evidence that coating does *not* materially affect the basic and novel characteristics of the claimed invention. DePuy Mitek cannot defeat summary judgment by criticizing defendants' evidence; it must produce its own genuine evidence of no material effect to defeat the motion. *See Univ. of Florida Research*

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[7] We do know that DePuy Mitek did at least perform pliability tests on coated and uncoated FiberWire, but claimed privilege and steadfastly refused to produce the results. Ex. 7 at Tab 48.

[8] DePuy Mitek asserts that the universal evidence of the affect of coating presented by defendants (which does not distinguish between types of coating) did not specifically state that those effects apply to silicone coating, such as used on FiberWire. DePuy Mitek Opp. at 17-18. DePuy Mitek, however, offers no evidence that the effects are different for silicone coating because there is none. In any event, to put the matter to rest, defendants submit additional evidence showing the obvious, that the handleability affects of coating are the same for silicone coating. Ex. 8 at col. 9, ll. 41-43; Ex. 9 at col. 9, ll. 40-42.

Foundation, Inc. v. Orthovita, Inc. 1998 WL 34007129 (N.D. Fla., April 6, 1998) at * 23 ("while Plaintiffs vigorously contend that Defendants' proffered sieve testing data is disputed and unreliable, in contravention of their burden in establishing infringement by a preponderance of the evidence, they have failed to produce *any* independent evidence that, using sieving, the Defendants' BioGran consists 'essentially of' bioactive glass particles . . . such that it infringes Claim 1;" summary judgment of non-infringement granted).

The rest of DePuy Mitek's arguments do nothing to create a *genuine* dispute of material fact. DePuy Mitek tries to create a disputed issue of fact by pointing to the testimony of Dr. Burks, one of defendants' experts. As explained above, DePuy Mitek's argument is irrelevant because DePuy Mitek cannot defeat summary judgment by criticizing defendants' evidence. Moreover, DePuy Mitek's reliance on Dr. Burk's tests does not excuse DePuy Mitek's failure to dispute the overwhelming, and undisputed, evidence of the universally-accepted reasons why coating is added to suture.

It comes as no surprise that DePuy Mitek, to be generous, is highly selective in its citation to Dr. Burks' testimony. Most importantly, DePuy Mitek "forgets" to inform the Court that Dr. Burks got the test right *all six times* he performed the tests both at his deposition and in preparation of his report. Ex. 10; Ex. 11 at 97:10-14, 20-23. Moreover, Dr. Burks never said he "could not clearly feel a difference" between the two sutures, as DePuy Mitek would have the Court believe. Rather, Dr. Burks stated that he was able to feel that the coated sutures were "generally smoother" than the uncoated sutures. Ex. 11 at 87:10-13. Read in the proper context, Dr. Burks merely testified to the obvious; if he did *a hundred* tests, he might not get it correct *every time*. DePuy Mitek Opp. at 16. There is no genuine dispute of material fact.

Likewise, DePuy Mitek cannot create a genuine issue of material fact by relying on the testimony of Dr. Brookstein. First, as defendants pointed out in their Opening Memorandum,

and which DePuy Mitek does not dispute, Dr. Brookstein is unqualified to testify on the issue of suture coating. He only worked on one suture project in his professional life and he could not remember if it involved issues of coating, and he was unable to confirm or deny the universal teachings about the effects of coating shown in the numerous patents and publications placed before him. Def. S. J. Mem. at 15 n.17.

In any event, there is nothing presented by DePuy Mitek's recitation of Dr. Brookstein's testimony that creates a disputed issue of fact. The only "evidence" cited by DePuy Mitek is Dr. Brookstein's observation "that the silicone was present in small amounts and did not substantially penetrate the braid and create a monofilament like structure." DePuy Mitek Opp. at 17. But the purported relevance of these observations is to support Dr. Brookstein's opinion that "regardless of FiberWire's coating, FiberWire is still 'two dissimilar yarns braided together to achieve improved handleability or pliability without significantly sacrificing its physical properties.'" DePuy Mitek Opp. at 17. As defendants explained in their Opening Memorandum at 16-17, this is Dr. Brookstein's "magic" and "miracles" argument where coating could only affect the basic and novel characteristics if "the coating in some *miraculous* way made those materials not yarns anymore" or "all of a sudden you had a set from A, a set from B and now if was some *magical* structure that wasn't yarns, it wasn't two sets, they were all the same, that would be a transformation." Ex. 5 at 398-399.

The undisputed evidence also shows that there is no basis for Dr. Brookstein's conclusion that the coating was present on FiberWire only in a "small amount." DePuy Mitek Opp. 17. Once again, DePuy Mitek fails to inform the Court of the pertinent and undisputed facts. While Dr. Brookstein's analysis showed that the coating constituted 3.4% volume of the FiberWire suture, he provided no basis for his conclusion that this is a "small" amount. All the *evidence* is to the contrary. The patents in the field, including a patent of DePuy Mitek's other expert, Dr.

Hermes, establishes the amount of coating typically on suture and necessary to achieve the handleability improvements is much, much less than the 3.4% reported by Dr. Brookstein. Ex. 12 at col. 2, ll. 46-49 (disclosing about 0.01 to about 0.1 weight percent coating, and preferably about 0.02 to about 0.5 weight percent coating); Ex. 13 at col. 3, l. 62 – col. 4, l. 1 (shows coating compositions in the amount of up to 0.25% by weight). Thus, the *undisputed evidence* is that Dr. Brookstein's 3.4% is a *large and more than sufficient amount* of coating to achieve handleability improvement, not the unsupported small amount. Unsupported conclusions, such as that submitted by the unqualified Dr. Brookstein, do not create a genuine dispute of material facts to defeat a motion for summary judgment. *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1080-81 (Fed. Cir. 2005).

DePuy Mitek's reliance on its patent to create an issue of material fact (DePuy Mitek Opp. at 18-19) is makeweight. Significantly, DePuy Mitek never disputes the law -- that unlisted materials can affect the basic and novel characteristics of the claimed invention even though the patent says that the unlisted materials can be used. Likewise, DePuy Mitek never disputes defendants' demonstration that the passage of the patent that says that coating can optionally be added unambiguously states that its invention allows the public to "eliminate[]" coating to "avoid[]" the costs and problems associated with coating. Def. S. J. Mem. at 18-19. Once again, there is no dispute of material fact.[9]

Finally, DePuy Mitek argues that the Court should reject defendants' argument that it is entitled to summary judgment even if the Court adopts Mitek's construction of the basic and novel characteristics (DePuy Mitek Opp. at 19), even though DePuy Mitek had twice told the

[9] Without support, DePuy Mitek asserts that the '446 patent only criticizes undefined "heavy coatings" and not FiberWire's type of coating. DePuy Mitek Opp. at 18. DePuy Mitek apparently forgets that the '446 patent criticizes "thermoset" coatings "which require[] a curing step for proper application." Ex. 4 at col. 1, ll. 52-54. FiberWire's coating is also a thermoset coating. Ex. 14 at 95:5-7.

Court that defendants had made no such argument. DePuy Mitek Opp. at 1, 14-15. Should the Court overlook DePuy Mitek's duplicity, there still is nothing to DePuy Mitek's argument. All DePuy Mitek says is that defendants "offer no evidence of any such effects." DePuy Mitek Opp. at 19. DePuy Mitek is wrong. Defendants' argument is copiously based on the *evidence* in the case, including DePuy Mitek's expert's own testimony that PET is added to FiberWire to improve the suture's knot tying ability. And then, defendants cite to the undisputed evidence that coating improves such characteristics. *See* Def. S. J. Mem. at 16 n.18. DePuy Mitek never disputes this evidence. Accordingly, it is DePuy Mitek, not defendants, who are making arguments without record support.

IV. SHOULD THE COURT CONSTRUE PE TO INCLUDE UHMWPE, THE '446 PATENT CLAIMS ARE INVALIDATED BY THE '575 PATENT

A. DePuy Mitek Has Not Disputed Defendants' Undisputed Facts That The '575 Patent Is Prior Art

As defendants explained in their Opening Memorandum, and DePuy Mitek does not dispute, the '575 patent application was filed before the '446 application and constitutes prior art unless DePuy Mitek can show that the claimed invention of the '446 patent was both conceived of and reduced to practice prior to the filing date of the '575 patent. Def. S. J. Mem. at 20.

Defendants also showed that the law requires that what was constructed by the patent applicant must meet *all* limitations of the claims, and that the undisputed facts are that Ethicon never did this because the claims of the '446 patent require sterilization and the braids that Ethicon built were never sterilized. Def. S.J. Mem. at 20-21. DePuy Mitek never says that defendants misstate the law, nor does it in any way dispute the fact that the Ethicon braids were not sterilized. DePuy Mitek's failure to dispute the law or these dispositive facts is a complete answer to DePuy Mitek's attempt to create a factual dispute.

The few things that DePuy Mitek does say are irrelevant. DePuy Mitek contends that there was no need for Ethicon to sterilize the braids because the testing performed was to prove the invention worked for its intended purpose. But the reduction to practice law requires *both* that the embodiment that is built meets all the limitations of the claims *and* that it be shown that the invention would work for its intended purpose. *See, e.g., Slip Track Sys., Inc. v. Metal-Lite, Inc.*, 304 F.3d 256, 1265 (Fed Cir. 2002). Whatever relevance DePuy Mitek's argument may have to the *second* prong (that the invention works for its intended purpose), it is irrelevant to the first prong and does not change the undisputed facts showing that the braids that Ethicon built did not meet all the limitations of the claims.[10] Accordingly, the '575 patent is prior art.[11]

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[10] For the same reason, DePuy Mitek's reliance of *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572 (Fed. Cir. 1996), is misplaced. That case only considered whether the evidence showed that the invention worked for its intended purpose. *Id.* at 1578. The case simply did not consider the issues whether the embodiment that was built met all the limitations of the claim.

[11] Even though DePuy Mitek's interrogatory answers only presented facts to support a contention that Ethicon actually reduced its invention to practice by actually building a prototype (Ex. 15 at 7-9; Ex. 16 at 9-10)**,** DePuy Mitek now, for the first time, tries to present evidence that Ethicon constructively reduced its invention to practice by diligence before the '575 patent application was filed. DePuy Mitek Opp. at 28-29. It is too late in the game for such a belated argument to be presented and should be summarily rejected.

In any event, DePuy has not created a genuine dispute of material fact. DePuy Mitek tries to establish its diligence is that a draft patent application was sent to an inventor in January 1992 and that Mr. Goodwin (the patent attorney) acted with diligence because he tried to get comments. But DePuy Mitek never produced the alleged draft application, so we have no way of knowing what was in the application and what relationship it has to the application as filed. Mr. Goodwin, the alleged actor, could not testify that he acted diligently because he did not remember if there was a draft application and had no idea if he ever prepared one or got any comments from the inventors. Ex. 17 at 77:18-21; 78:4-7. Moreover, a document that DePuy Mitek did produce that discusses actions by Ethicon conclusively shows the *opposite* of diligence; it shows that Ethicon delayed, delayed and delayed. Ex. 18. Finally, DePuy Mitek even gets the date to which it must show diligence wrong because the undisputed evidence of record shows that the '575 patent was conceived of a year or more before the '575 patent application was filed. Ex. 19 at 33:15-34:4. Accordingly, Ethicon has no evidence to establish a genuine dispute of material fact.

B. There Is No Genuine Dispute Of Material Fact That The‘575 Patent Invalidates The Asserted Claims Of The ‘446 Patent

Defendants meticulously went through each and every limitation of the asserted claims of the ‘446 patent and demonstrated where each limitation was shown in the ‘575 patent (should the Court disagree with defendants’ claim interpretation and find that UHMWPE is included within the definition of “PE” as used in the ‘446 patent). Def. S. J. Mem. at 21-27. In its Opposition, DePuy Mitek largely ignores the presentation made by defendants, hardly saying a word as to why, at least in DePuy Mitek’s view, defendants’ assertions are wrong. Instead, DePuy Mitek reverts to some of its favorite tactics -- misstate defendants’ argument, ignore the testimony of its own expert, or both.

DePuy Mitek bases its argument on a false premise. It asserts that “Arthrex’s argument focuses on the spiroid braided construction depicted in Figure 6 of the 575 patent” and then tries to show that that figure does not anticipate the claims of the ‘446 patent. DePuy Mitek Opp. at 22-24. But that is *not* defendants’ argument. Defendants point to Figure 6 for the sole purpose of showing an additional example of direct intertwining contact (Def. S. J. Mem. at 23), a fact that even DePuy Mitek does not dispute. Rather, defendants’ argument is based on claim 11 or 12 of the ‘575 patent, dependant claims that also include claim 1. When defendants’ argument is put into *proper* focus, *not* the misdirection attempted by DePuy Mitek, DePuy Mitek’s argument becomes a house of cards that falls apart.

DePuy Mitek makes the unfathomable argument that the ‘575 patent does not disclose a suture, relying on the alleged opinion of Dr. Hermes that claims of the ‘575 patent disclose a sternum device. DePuy Mitek Opp. at 23. But DePuy Mitek has no answer to the undisputed evidence that the ‘575 patent refers to every embodiment (called an elongated structure in the claims of the ‘575 patent) as a suture (Ex. 20 at Title, col. 1, l. 7, col. 2, l. 62 – col. 3, l. 19, col.

5, l. 55, col. 7, l. 26, 43, 50, col. 8, l. 23) and that Dr. Hermes admitted that the disclosed elongated structures are called sutures in the '575 patent. *See* Def. S. J. Mem. at 22.[12]

While DePuy Mitek tries to imply that the claims of the '575 patent do not disclose the combination of UHMWPE and PET (or nylon), it never says so because any such assertion would have no basis in the evidence. As defendants' demonstrated, *and DePuy Mitek cannot deny*, claim 11 (which incorporates claim 1) discloses UHMWPE and nylon, and claim 12 (which also incorporates claim 1), discloses UHMWPE and PET.[13]

DePuy Mitek's contention that the claims of the '575 patent do not disclose the two materials in direct intertwining contact also ignores the undisputed evidence presented by defendants. Claim 1 of the '575 patent states that the two materials "are braided to form" the elongated member. Ex. 20 at col. 8, ll. 37-38. DePuy Mitek does not dispute that Dr. Hermes could not provide a single example of a braided construction that was not braided in direct intertwining contact. Def. S.J. Mem. at 24. The undisputed facts are that the two materials have to be braided in direct intertwining contact.[14]

DePuy Mitek's brief reference to sterilization is wholly without merit. DePuy Mitek does not dispute that the patent disclosed in the '575 patent explicitly discloses sterilization, nor does it present any legal authority that such a disclosure is insufficient. Moreover, DePuy Mitek does

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[12] DePuy Mitek's assertion that Mr. Soffen, Arthrex's counsel "advised Arthrex that the 575 Patent claims do not describe the use of suture" (DePuy Mitek Opp. at 23 n. 13) is not true. All Mr. Soffen advised his client was that the use described in the claims of the 575 patent were different from the uses of FiberWire and thus, FiberWire did not infringe the claims of the '575 patent. Ex. 21. He *never* said that "the 575 Patent claims do not describe the use of a suture" and DePuy Mitek points to *no* evidence where such a statement was made.

[13] The parties do agree that the disclosure of polyester in claim 12 is a disclosure of PET.

[14] DePuy Mitek's reference to the "core/sheath arrangement [of] Figures 8 and 9" cannot create a factual dispute. Dr. Hermes admitted that claim 1 of the '575 patent included configurations where there was no core. Ex. 22 at 199:14-18. Thus, DePuy Mitek's reference to Figures 8 and 9 is of no help to DePuy Mitek because the claims of the '575 patent, as DePuy Mitek's own expert admitted, include configurations other that the core/sheath arrangement of Figures 8 and 9.

not present any evidence to dispute the known FDA requirement that a suture must be sterilized before use. Ex. 23 at ¶ 14 and Ex. E, thereto. Thus, sterilization obviously would be known to one of ordinary skill in the art reading the '575 patent, all that is required for the limitation to be present. *See, e.g., Fenton Golf Trust v. Cobra Golf, Inc.*, 1998 U.S. Dist. LEXIS 8452, *9-*14 (E.D.Ill. 1998).

In trying to create a disputed issue of fact about the "volume fraction" limitation added by claim 9 of the '446 patent, DePuy Mitek again chooses to ignore the undisputed evidence that the '575 patent discloses combinations that include a volume fraction of the first fiber-forming material between about 20-80%. Def. S. J. Mem. at 26. Unable to respond, DePuy Mitek tries to change the question and asserts that defendants' must show that the '575 inherently discloses a volume fraction of between 20-80%. But DePuy Mitek presents no reason why it is raising the law of inherency. There is no reason to do so (except to try to create confusion) because the '575 patent discloses embodiments that fall within the 20-80% range. That is all that is required, and DePuy Mitek never presents any reason why that is not a sufficient disclosure.

Finally, perhaps because it cannot dispute the undisputed facts presented in defendants' motion, DePuy Mitek chooses to begin its discussion of the '575 patent with an argument that summary judgment should be denied because defendants' argument here is different from Arthrex's description of the '575 patent when it was seeking its FiberWire patent. DePuy Mitek Opp. at 21-22. Even if DePuy Mitek were correct – and it decidedly is not – it would be irrelevant because the only relevant issue is the comparison of the disclosure of the '575 patent and the asserted claims of the '446 patent.

There is no basis for DePuy Mitek's accusation. According to DePuy Mitek, Arthrex's counsel allegedly told the Patent Office that the '575 patent does not disclose an example of a braided sheath that includes both UHMWPE and polyester. DePuy Mitek Opp. at 22. DePuy

Mitek can only make such an assertion by taking the statements completely out of context. The claims in the FiberWire patent describe a core of UHMWPE surrounded by a braided sheath (called a "cover" in the claims) of UHMWPE and polyester. Ex. 24 at col. 3, l. 13 – col. 4, l. 23. In distinguishing *this* configuration from the '575 patent, Arthrex's counsel correctly stated that examples discussed in the '575 patent not do not disclose a core of UHMWPE and a braided sheath which included both UHMWPE and polyester. Ex. 25 at 5. Arthrex's counsel was silent on the specific issue involved here, that is, the combination of a braid of UHMWPE and polyester without the need for a core, which is confirmed by the testimony of Arthrex's counsel. Ex. 26 at 107:6-20. Accordingly, there is no inconsistency despite DePuy Mitek's effort to create one.

Dated: September 15, 2006

Respectfully submitted,

By:/s/Charles W. Saber

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that a true and correct copy of the foregoing Defendants Arthrex, Inc.'s and Pearsalls, Ltd.'s Reply Memorandum in Support of Their Motion for Summary Judgment was served, via the Court's email notification system on the following counsel for Plaintiff on the 15th day of September 2006:

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/s/Charles W. Saber

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. **a Massachusetts Corporation** **Plaintiff,** **v.** **Arthrex, Inc.** **a Delaware Corporation and** **Pearsalls Ltd.,** **a Private Limited Company** **of the United Kingdom,** **Defendants.**	)	**Civil No. 04-12457 PBS**

Expert Report of Dr. David Brookstein

I. Background Information

A. Teaching Experience

1. I am the Dean and Professor of Engineering at the School of Engineering and Textiles of Philadelphia University. I have held this position since 1994. In 2005, I also was appointed Executive Director of Research at Philadelphia University.

2. I was a Visiting Scholar at the Harvard University Center for Textile and Apparel Research (Division of Engineering and Applied Sciences) between 2002-2003.

3. I was an Adjunct Professor in Mechanical Engineering at Northeastern University in Boston, MA from 1981-1983. At Northeastern, I taught undergraduate courses in statics, dynamics, and mechanics of deformable bodies and material science.

4. I was Assistant Professor of Textile Engineering at Georgia Institute of Technology, College of Engineering from 1975 – 1980. At Georgia Tech, I taught and

polyethylene (*i.e.*, including UHMWPE), then it is my opinion that there is infringement under the doctrine of equivalents because any differences are insubstantial.

53. I have used the "function/way/result" test to determine infringement of claims 1, 2, 8, 9, and 12 under the doctrine of equivalents. In particular, I have determined the function/way/result of the claim element that Arthrex contends is not literally satisfied and compared that to the function/way/result of UHMWPE in FiberWire™ and TigerWire™.

54. In my opinion, the "function" of the first fiber-forming material is the same as the function of UHMWPE in Arthrex's FiberWire™ and TigerWire™ suture products:

Claims 1, 2, 8, 9, and 12 Limitation	**Function of Limitation Under the Doctrine of Equivalents**	**Function of UHMWPE in FiberWire™ and TigerWire™ Suture Products**
a) each yarn from the first set is composed of a plurality of filaments of a first fiber-forming material selected from the group consisting of PTFE, FEP, PFA, PVDF, PETFE, PP and PE; and	The function of the first set of yarns is to contribute a property that is different than a yarn from the second set.	UHMWPE contributes different lubricity and strength properties to the heterogeneous braid than PET.

55. My opinion regarding the "function" of the first fiber-forming material is supported by the '446 Patent. The '446 Patent explains that the first fiber forming material is "dissimilar" to the second fiber and the braid of dissimilar yarns provides "outstanding properties attributable to the specific properties of the dissimilar fiber-forming materials which make up the braided yarns" (Tab D at 2:50-52; 3:43-48). Further, the '446 Patent explains that it is possible to "tailor the physical" properties by "varying the type and proportion of each of the dissimilar fiber forming materials used" (Tab D at 2:58-61). Further, the patent notes that the different fiber components make different relative contributions to one or more properties of the heterogeneous braid (Tab D at 8:19-21).

56. It is my opinion that the UHMWPE in Arthrex's FiberWire™ and TigerWire™ products has the function as the claimed first fiber-forming material based on an examination of FiberWire™ and TigerWire™ and its manufacturing. In my opinion, the UHMWPE contributes a property or properties that is/are different from the property or properties contributed by the PET. For example, Mr. Hallet testified that, in the development of FiberWire™, he had constructed a 100% homogeneous UHMWPE braid, but Arthrex had requested a less stiff braid. Mr. Hallet then made a heterogeneous braid of UHMWPE and PET to get the strength of UHWMPE and the flexibility of PET (Hallet 1/12/06 Dep. at p. 306:17-307:14; DMI Ex. 324; *see also* Hallet 1/12/06 Dep. at p. 307:15-308:14; DMI Ex. 325).

57. In my opinion, the "way" of the first fiber-forming material is the same as the "way" of UHMWPE in Arthrex's FiberWire™ and TigerWire™ suture products:

Claims 1, 2, 8, 9, and 12 Limitation	**"Way" of Limitation Under the Doctrine of Equivalents**	**Way UHMWPE performs its Function in FiberWire™ and TigerWire™**
a) each yarn from the first set is composed of a plurality of filaments of a first fiber-forming material selected from the group consisting of PTFE, FEP, PFA, PVDF, PETFE, PP and PE; and	The "way" is at least one yarn from the first set of yarns is in direct intertwining contact with at least one yarn from the second set.	At least one UHMWPE yarn is braided with at least one PET yarn in direct intertwining contact (Dreyfuss 9/16/05 Dep. at p. 99-107).

58. My opinion regarding the "way" of the "first fiber-forming" element is supported by the '446 Patent. The '446 Patent explains that the way that the first-fiber forming material performs its function is by braiding it with a second dissimilar yarn in direct intertwining contact For example, the '446 Patent states in the "Summary of the Invention" section that the "the invention is a heterogeneous braid comprising a first and second set of discrete yarns in a sterilized, braided construction" and that the at least one yarn from the first set is in "direct

intertwining contact" with a yarn from the second set (Tab D at 2:40-44; *see also* 3:21-28; 3:40-45). The '446 Patent further explains that the heterogeneous braid properties are due to the "mechanical interlocking or weaving of the individual yarns" (Tab D at 2:56-58; 3:43-48). Also, during the prosecution history, the applicants explained that the beneficial properties are due to the braiding of direct "intertwining" contact of dissimilar yarns (December 2, 1992 Office Action at 2, emphasis original).

59. Further, the '446 Patent describes certain preferred embodiments in which the first fiber-forming materials act as lubricating yarns and the second fiber-forming materials provide strength (Tab D at 4:9-59). The '446 Patent also describes other specific preferred embodiments that have PTFE braided in direct intertwining contact with PET to obtain the benefits of each yarn (Tab D at 7:1-8:61). These are all preferred embodiments where the at least one first-fiber forming material is braided in direct intertwining contact with at least one different, second fiber-forming material so that each yarn contributes to the heterogeneous braid. Because these are preferred embodiments, they are an example of the broader disclosed concept of braiding the first and second fiber forming materials so that they can individually contribute to the overall properties of the heterogeneous braid. Notably, the invention is described more broadly than just these "preferred embodiments," and, therefore, it is my opinion that neither the function, way, or result is limited to the specific properties of the first-forming material in any of the preferred embodiments.

60. It is my opinion that the UHMWPE in Arthrex's FiberWire™ and TigerWire™ suture products have the same "way" as the claimed first-fiber forming materials. My opinion is based on a visual inspection and observation of FiberWire™ and its manufacturing processes. In my opinion, at least one UHMWPE yarn in Arthrex's FiberWire™ and TigerWire™ products is

braided in direct intertwining contact with at least one PET yarn. My opinion is supported by Arthrex's and Pearsalls' testimony and documents. For example, Mr. Dreyfuss testified that the adjacent yarns in the FiberWire™ and TigerWire™ sheath are in direct intertwining contact with each other (Dreyfuss 9/16/05 Dep. at p. 99-107).

61. In my opinion, the "result" of the first forming material is the same as the result of UHMWPE in Arthrex's FiberWire™ and TigerWire™ suture products:

Claims 1, 2, 8, 9, and 12 Limitation	**"Result" of Limitation Under the Doctrine of Equivalents**	**Result of UHMWPE in FiberWire™**
a) each yarn from the first set is composed of a plurality of filaments of a first fiber-forming material selected from the group consisting of PTFE, FEP, PFA, PVDF, PETFE, PP and PE; and	The result of the first set of yarns is to contribute to the heterogeneous suture braid a property different from the yarn in the second set, so that when they are braided the yarns contribute to the properties of the overall heterogeneous braid.	The result of the PE yarns is to provide a different property than the PET, so that when they are braided the PE yarns contribute properties to the overall heterogeneous braid.

62. My opinion regarding the "result" of the first-forming material is supported by the '446 Patent. For example, the '446 Patent explains that the "heterogeneous braids may exhibit a combination of outstanding properties attributable to the specific properties of the dissimilar fiber-forming materials" (Tab D at 2:49-52). Further, the '446 Patent states that the "types of yarns used to prepare the heterogeneous braid and the yarn geometry can be varied to prepare heterogeneous braids within the scope of the claimed invention which exhibit a combination of outstanding physical or biological properties." (Tab D at 1:51-56).

63. My opinion is that FiberWire™ and TigerWire™ suture products have the same claimed result. UHMWPE has and contributes properties that are different from those provided by PET. For example, Arthrex has admitted that the UHMWPE is added to FiberWire™ to increase strength. (Arthrex supplemental response to Interrogatory No. 3) In FiberWire™, when

the UHMWPE is braided with PET, it is my opinion that the UHMWPE contributes to the strength of the overall heterogeneous braid. Further, UHMWPE is known to have relatively high lubricity and has different lubricity than PET.

64. My opinion is further supported by the testimony and documents from Arthrex and Pearsalls witnesses:

> Q What did you understand Mr. Grafton to mean when he said:
> "Can you build a 25% Dyneema/75% polyester blend in Size 2 that is very flexible".
> What did you understand that to mean?
> A Yes, that he wanted a braid which was more -- not so stiff.
> Q As the 100% ultra high molecular weight polyethylene?
> A Yes. (Hallet 1/12/06 Dep. at p. 306:20-307:4, DMI Ex. 324)

> Q. Mr. Grafton wanted Pearsalls to braid polyester with the ultra high molecular weight polyethylene so that the polyester could provide flexibility?
> A Yes. (Hallet Dep. at p. 307:10-14, DMI Ex. 324)

65. It is my expert opinion that both of the above documents and testimony demonstrate that Arthrex is "tailor[ing] the physical" properties of the braid by "varying the type and proportion of each of the dissimilar fiber forming materials used" as taught by the '446 Patent (Tab D at 2:58-61).

66. In summary, if it is determined that PE is not PE (does not include UHMWPE), it is my opinion that the ultra high molecular weight polyethylene in Arthrex's FiberWire™ and TigerWire™ suture products is equivalent to the claimed PE because it performs the same function, in the same way to achieve the same result. Any differences are insubstantial in the context of the invention.

Dated: March 3, 2006

David Brookstein, Sc.D.
Fellow-American Society of Mechanical Engineers

EXHIBIT 2

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. **a Massachusetts Corporation** **Plaintiff,** **v.** **Arthrex, Inc.** **a Delaware Corporation and** **Pearsalls Ltd.,** **a Private Limited Company** **of the United Kingdom,** **Defendants.**	)	**Civil No. 04-12457 PBS**

Declaration of Dr. David Brookstein In Support of DePuy Mitek's
Claim Interpretation of the Hunter Patent and Summary Judgment of Infringement

I. Background Information

A. Teaching Experience

1. I am the Dean and Professor of Engineering at the School of Engineering and Textiles of Philadelphia University. I have held this position since 1994. In 2005, I also was appointed Executive Director of Research at Philadelphia University.

2. I was a Visiting Scholar at the Harvard University Center for Textile and Apparel Research (Division of Engineering and Applied Sciences) between 2002-2003.

3. I was an Adjunct Professor in Mechanical Engineering at Northeastern University in Boston, MA from 1981-1983. At Northeastern, I taught undergraduate courses in statics, dynamics, and mechanics of deformable bodies and material science.

4. I was Assistant Professor of Textile Engineering at Georgia Institute of Technology, College of Engineering from 1975 – 1980. At Georgia Tech, I taught and conducted research in

polyester (Ex. 4 at 2:50-57). As the 234 patent explains, braiding polyester with UHMWPE improves knot tie down characteristics or the "ability to approximate the tissue and hold it in place through biomechanical forces" (Ex. 3 at 26:24-27:10). Thus, the 234 patent teaches that polyester, which includes materials such as PET, imparts knot tie down or knot holding strength to a braid of UHMWPE and polyester. Thus, Arthrex's 234 Patent further shows that the differences are insubstantial because UHMWPE is described as a lubricous yarn that with bad knot properties, and similarly embodiments of the first fiber-forming materials are described as lubricous.

20. I understand that Arthrex has asserted that the differences between the first fiber-forming materials (if PE does not include UHMWPE) and UHMWPE are substantial because the purpose of UHMWPE in FiberWire is alleged to be to provide strength (Arthrex Br. at 11). I disagree with this statement because the 446 Patent describes embodiments in which the first set of yarns is lubricous and provides PE as an example of a lubricous yarn (Ex. 2 at 4:11-12). The UHMW PE in FiberWire is consistent with this description; FiberWire's UHMW PE is lubricous (Ex. 3 at 52:24-53:1). The 446 Patent also describes embodiments in which the claimed second fiber-forming yarns, including PET, are braided with the claimed first fiber-forming lubricous yarns, including PE, "to provide improved strength to the heterogeneous braid" (Ex. 2 at 4:33-36). FiberWire is consistent with this description; FiberWire's PET has a different lubricity than UHMWPE and adds improved strength to the FiberWire braid (Ex. 3 at 53:20-54:5; 46:16-47:5). Accordingly, PET increases certain knot strength properties, namely knot holding strength,[2] of

[2] I use the term "knot pull strength" to refer to the force at which a suture having a knot tied in it fails when tested in a tension test. I use the term "knot holding strength" to refer to the force at which a knot fails by slipping, elongating to a certain extent, or breaking, which can be tested generally in a procedure similar to Exs. 26 and 27. Knot holding strength is an indication

the braid of PET and UHMWPE because it reduces the tendency of the UHMWPE fibers to slip when tied in a knot. Thus, because FiberWire's UHMWPE is lubricous and FiberWire's PET imparts strength, FiberWire's construction is not the opposite of that described and claimed in the 446 Patent. Rather, it is consistent with the 446 Patent's teachings.

B. The Differences Between the Claimed First Fiber-Forming Materials And FiberWire's PE Are Insubstantial Based On the Function/Way/Result Analysis

21. It is my opinion that all of Arthrex's FiberWire™ and TigerWire™ suture products also infringe claims 1, 2, 8, 9, and 12 of the '446 Patent under the doctrine of equivalents because the differences, if any, between the claims, as I understand they may be construed by Arthrex, and Arthrex's FiberWire™ and TigerWire™ suture products are insubstantial under the function/way/result analysis.

22. I have used the "function/way/result" test to determine infringement of claims 1, 2, 8, 9, and 12 under the doctrine of equivalents. In particular, I have determined the function/way/result of the claim element that Arthrex contends is not literally satisfied and compared that to the function/way/result of UHMWPE in FiberWire™ and TigerWire™. My equivalency opinion is limited to nonbioabsorbable yarns as the first-forming material.

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of knot security. The 446 Patent describes another exemplary knot security test (Ex. 2 at 6:36-44).

64. It is my expert opinion and observation that the coating only appears on the surface of the braid.

I declare under penalty of perjury that the foregoing is true and correct.

Date Executed: September 1, 2006 /s/

EXHIBIT 3

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc., a Massachusetts Corporation,

Plaintiff,

vs.

Arthrex, Inc., a Delaware Corporation,

Defendant.
_____/

COPY

CIVIL ACTION
NO. 04-12457 PBS

DEPOSITION OF:	DONALD GRAFTON
DATE:	March 14, 2006
TIME:	8:38 a.m. to 1:23 p.m.
LOCATION:	The Ritz Carlton Golf Resort 2600 Tiburon Drive Naples, FL 34112
TAKEN BY:	Plaintiff
REPORTER:	Deborah A. Krotz, RPR, CRR
VIDEOGRAPHER:	Gene Howell, CLVS

Deberdino who was a surgeon at Fort Sam Houston, San Antonio. His -- his comments were that he had tied three knots the previous afternoon using the FASTak product of Arthrex -- that's a glenoid labrum device -- and had broke the knots on all three of them. And -- you know -- he said it kind of jokingly. He said, "And I didn't even work out the day before."

And so he was tying to be nice about it, but bottom line was your suture sucks. Okay?

And so -- you know -- we're in a position where we need to find a suture that will be competitive. I had been to Pearsalls many times working on bioabsorbable products. This was the time that you referred to earlier where I said three to five, and was familiar with suture manufacturing, the steps required to manufacture a suture.

One of the trips there, Mr. Lyon had pointed out to me a -- the other products they manufactured, which was fishing line and silk used in decorated drapes. The fishing line used a ultra-high molecular weight polyethylene material that was very strong, and I -- at some point, it was decided that we would try some of that for a suture.

I had Pearsalls, mainly through Brian, as being the manufacturing person --

Q. Brian Hallett?

A. That's correct -- make some Size 2 braided material, send to me, and at the -- coincidentally, at the same time, I had a Dr. Steve Burkhart from San Antonio and a Dr. Casey Chan, who is a R & D guy in knot testing and suture. They were -- they were at Arthrex at the time when this material showed up.

We tested the material. The strength was excellent. The knot slippage was very poor, would not hold a knot.

So at that point in time, it looked like we would not be able to use an alternative material of ultra-high molecular weight polyethylene because the slippage of the material -- because of the slippage of the material tested with Casey Chan -- Dr. Chan and Dr. Burkhart. And so at that point in time, the -- the product was -- was on hold.

I was on a trip to Chicago to the national sales meeting, and I had this idea of adding PET to the ultra-high molecular weight polyethylene to enhance the or reduce the knot slippage of the product. I sent an e-mail to Dr. Steve Burkhart and suggesting that since he was familiar with the testing we had done very recently with just the ultra-high molecular weight PE, of adding the PET, and his -- I'll never forget the e-mail. He thought that was a killer idea.

And so I had asked then at that time for Brian

A. Yes.

Q. And was the knot slippage of this ultra-high molecular weight polyethylene poor security because of the lubricity of polyethylene?

A. Yes.

Q. Yes?

A. Yes.

Q. So then you came up with the idea to braid PET with the ultra-high molecular weight polyethylene to reduce the knot slippage?

A. Yes.

Q. And when you say knot slippage, we're referring to this knot security test?

A. Yes.

Q. So are we using the terms knot slippage and knot security interchangeably here?

A. You are, yes.

Q. In your testimony?

A. Yes.

Q. So the knot security of the 100 percent ultra-high molecular weight polyethylene was poor, the prototype; right?

A. Yes.

Q. And your idea was to add the PET and to improve the knot security?

MR. SOFFEN: Objection; asked and answered. You've asked him the same thing multiple times. But you can answer.

A. I've lost count, it's been so many times, but the answer again is yes.

Q. Okay. And Dr. Burkhart said that was a killer idea?

A. What was a killer idea?

Q. The killer idea was that your idea of adding PED -- PET -- I'm sorry. I'll rephrase that question.

Did Dr. Burkhart say that your idea to braid PET with the ultra-high molecular weight polyethylene to improve knot security was a killer idea?

A. Yes.

Q. Okay. And then you said you had Pearsalls manufacture a prototype that had PET and ultra-high molecular weight polyethylene braided?

A. Yes.

Q. And you tested that prototype?

A. Yes.

Q. And you said that that prototype had good knot strength?

A. Correct.

Q. And the prototype of PET braided with ultra-high molecular weight polyethylene had good knot security?

EXHIBIT 4

US005314446A

United States Patent [19]

Hunter et al.

[11] Patent Number: 5,314,446

[45] Date of Patent: May 24, 1994

[54] **STERILIZED HETEROGENEOUS BRAIDS**

[75] Inventors: **Alastair W. Hunter**, Bridgewater; **Arthur Taylor, Jr.**, Plainfield, both of N.J.; **Mark Steckel**, Maineville, Ohio

[73] Assignee: **Ethicon, Inc.**, Somerville, N.J.

[21] Appl. No.: **838,511**

[22] Filed: **Feb. 19, 1992**

[51] **Int. Cl.**[5] **D04C 1/00**

[52] **U.S. Cl.** **606/231**; 606/228; 87/7; 87/9; 428/370

[58] **Field of Search** 606/228, 230, 231; 87/7, 8, 9; 428/225

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,187,752	6/1965	Glick	128/335.5
3,463,158	8/1969	Schmitt et al.	606/228
3,527,650	9/1970	Block	117/7
3,636,956	1/1972	Schneider	128/335.5
3,942,532	3/1976	Hunter et al.	128/335.5
4,043,344	8/1977	Landi et al.	128/335.5
4,047,533	8/1977	Perciaccante et al.	128/335.5
4,052,988	10/1977	Doddi et al.	128/335.5
4,141,087	2/1979	Shalaby et al.	3/1
4,470,941	9/1984	Kurtz	264/136
4,624,256	11/1986	Messier et al.	128/335.5
4,946,467	8/1990	Ohi et al.	606/228
4,959,069	9/1990	Brennan et al.	606/228
4,979,956	12/1990	Silverstrini	623/13
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5,147,400	9/1992	Kaplan et al.	623/13

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2949920	3/1981	Fed. Rep. of Germany	A61F 1/00
WO86/00020	1/1986	PCT Int'l Appl.	A61L 17/00
2082213	8/1980	United Kingdom	
2218312A	11/1989	United Kingdom	A01K 91/00

Primary Examiner—George F. Lesmes
Assistant Examiner—Chris Raimund
Attorney, Agent, or Firm—Hal Brent Woodrow

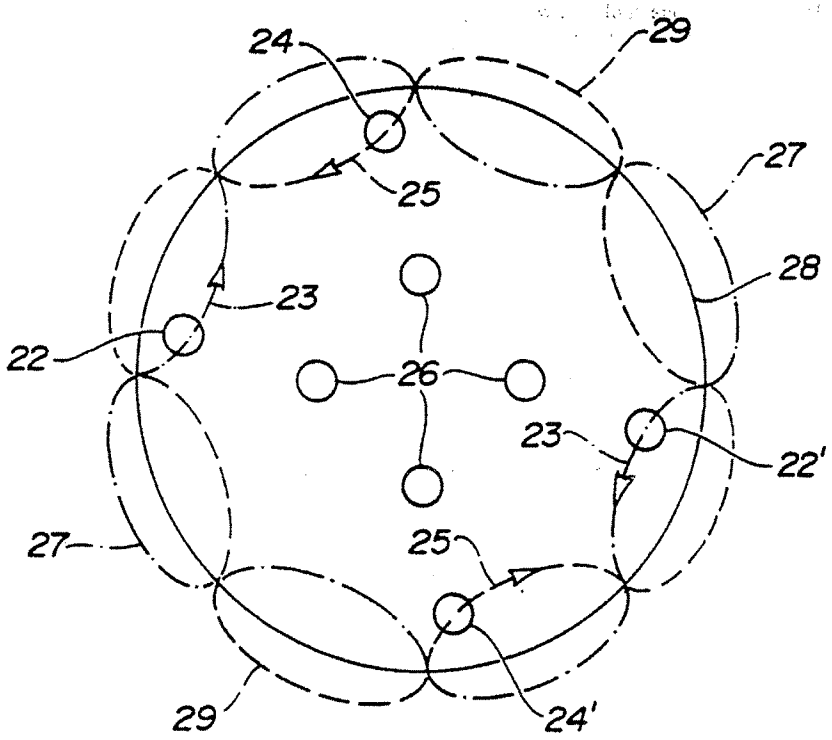
[57] **ABSTRACT**

Heterogeneous braided multifilament of first and second set of yarns mechanically blended by braiding, in which first and second set of yarns are composed of different fiber-forming materials.

Heterogeneous braids are useful for preparation of surgical sutures and ligatures.

12 Claims, 3 Drawing Sheets

FIG-1



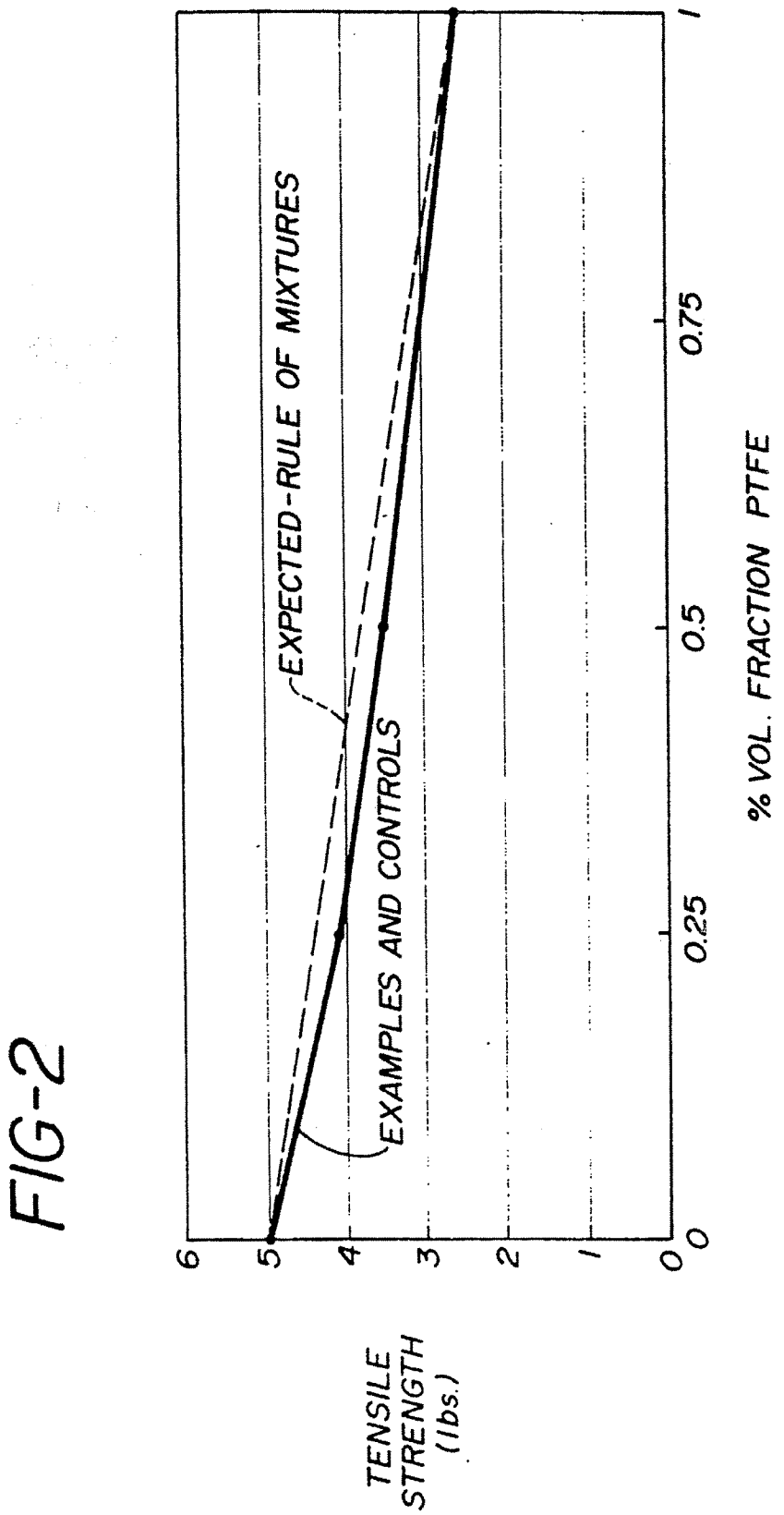
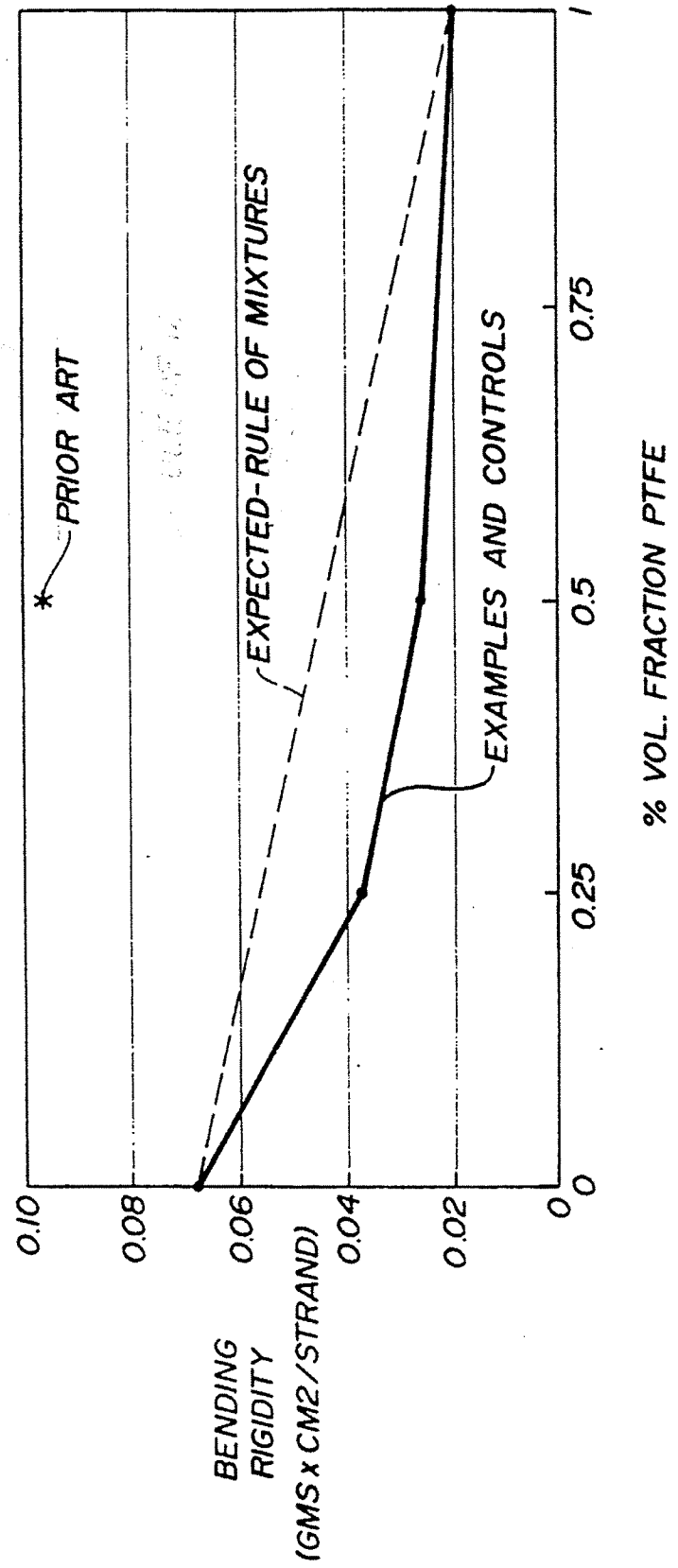

EXPECTED-RULE OF MIXTURES
EXAMPLES AND CONTROLS
TENSILE STRENGTH (lbs.)
6
5
4
3
2
1
0
0
0.25
0.5
0.75
1
% VOL. FRACTION PTFE

FIG-2

FIG-3


PRIOR ART
EXPECTED-RULE OF MIXTURES
EXAMPLES AND CONTROLS
BENDING RIGIDITY (GMS x CM2/STRAND)
0.10
0.08
0.06
0.04
0.02
0
0.25
0.5
0.75
1
% VOL. FRACTION PTFE

STERILIZED HETEROGENEOUS BRAIDS

BACKGROUND OF THE INVENTION

This invention relates to braided multifilaments, and especially to sterilized, braided multifilaments suitably adapted for use as surgical sutures or ligatures.

Braided multifilaments often offer a combination of enhanced pliability, knot security and tensile strength when compared to their monofilament counterparts. The enhanced pliability of a braided multifilament is a direct consequence of the lower resistance to bending of a bundle of very fine filaments relative to one large diameter monofilament. However, for this enhancement to be realized, the individual multifilaments must be able to bend unencumbered or unrestricted by their neighboring filaments. Any mechanism which reduces this individual fiber mobility, such as simple fiber-fiber friction, a coating which penetrates into the braid interstices, or a melted polymer matrix which adheres fibers together, will adversely affect braid pliability. In the extreme case where the multifilaments are entirely bonded together, the pliability or bending resistance closely approximates that of a monofilament.

Unfortunately, the prior art abounds with attempts to improve specific properties of multifilament braids at the expense of restricting the movement of adjacent filaments which make up the braid,. For example, multifilament sutures almost universally possess a surface coating to improve handling properties.

U.S. Pat. No. 3,942,532 discloses a polyester coating for multifilament sutures. The preferred polyester coating is polybutilate, which is the condensation product of 1,4-butanediol and adipic acid. U.S. Pat. No. 4,624,256 discloses a suture coating copolymer of at least 90 percent ϵ-caprolactone and a biodegradable monomer, and optionally a lubricating agent. Examples of monomers for biodegradable polymers disclosed include glycolic acid and glycolide, as well as other well known monomers typically used to prepare bioabsorbable coatings for multifilament sutures.

An alternative to the use of the commonly accepted coating compositions for multifilament sutures to improve handling properties is disclosed in U.S. Pat. 3,527,650. This patent discloses a coating composition of polytetrafluoroethylene (PTFE) particles in an acrylic latex. Although the PTFE particles act as an excellent lubricant to decrease the surface roughness of multifilament sutures, the particles have a tendency to flake off during use. Also, this particular coating is a thermoset which requires a curing step for proper application.

More recently, a dramatic attempt has been made to create a monofilament-like surface for a multifilament suture. U.S. Pat. No. 4,470,941 discloses the preparation of "composite" sutures derived from different synthetic polymers. The composite suture is composed of a core of low melting fibers around which are braided high melting fibers. Because of the lack of cohesiveness of the dissimilar fibers, the low melting fibers in the core are melted and redistributed throughout the matrix of the braided, high melting fibers. Although these composite sutures represent an attempt to combine the best properties of different synthetic fibers, it unfortunately fails in this respect due to increased stiffness (as evidenced by FIG. 3 which is described in detail below),

apparently due to the reduction of fiber mobility resulting from the fusing of the fibers together.

Another attempt to enhance the properties of multifilament sutures can be found in WO 86/00020. This application discloses coating an elongated core of a synthetic polymer having a knot tenacity of at least 7 grams/denier with a film-forming surgical material. The film-forming surgical material can be absorbable or nonabsorbable, and can be coated on the elongated core by solution casting, melt coating or extrusion coating. Such coated multifilament sutures suffer from the same deficiencies which plague conventionally coated multifilament sutures.

All of the attempts described in the prior art to improve braid properties have overlooked the importance of fiber-fiber friction and its impact on fiber mobility and braid pliability. The properties of concern here include the fiber-fiber frictional coefficients (which frequently relate to the polymer's surface energy), the fiber cross-sectional shape and diameter, and the braid structure which influences the transverse forces across the braid. If fibers composed of highly lubricous polymers are used in the traditional manner, then a highly pliable braid can be prepared. However, in most cases, these braids will be relatively weak and unusable. Hence, a tradeoff between braid strength and pliability exists in the design of conventional braided multifilaments.

In view of the deficiencies of the prior art, it would be desirable to prepare multifilament sutures exhibiting improved pliability and handling properties. More specifically, it would be most desirable to prepare braided multifilaments composed of dissimilar fiber-forming materials in which the fiber-forming materials contribute significantly to enhanced pliability for the braided multifilament without appreciably sacrificing its physical properties.

SUMMARY OF THE INVENTION

The invention is a heterogeneous braid comprising a first and second set of continuous and discrete yarns in a sterilized, braided construction. At least one yarn from the first set is in direct intertwining contact with a yarn from the second set.

Each yarn from the first set is composed of a plurality of filaments of a first fiber-forming material, and each yarn from the second set is composed of a plurality of filaments of a second fiber-forming material.

Surprisingly, the heterogeneous braids may exhibit a combination of outstanding properties attributable to the specific properties of the dissimilar fiber-forming materials which make up the braided yarns. The dissimilar fiber forming materials do not require melt bonding or any other special processing techniques to prepare the heterogeneous braids of this invention. Instead, the integrity of the braid and therefore its properties is due entirely to the mechanical interlocking or weaving of the individual yarns. In fact, it is possible to tailor the physical and biological properties of the braid by varying the type and proportion of each of the dissimilar fiber forming materials used, as well as adjusting the specific configuration of the braid. For example, in preferred embodiments, the heterogeneous braid will exhibit improved pliability and handling properties relative to that of conventional homogeneous fiber braids, without sacrificing physical strength or knot security.

The sterilized, heterogeneous braids of this invention are useful as surgical sutures or ligatures, as well as for

the preparation of any other medical device which would benefit from its outstanding physical or biological properties.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates a carrier layout for the preparation of a heterogeneous braid within the scope of this invention;

FIG. 2 is a plot representing the relationship between the tensile strength of heterogeneous and homogeneous braids of polyethylene terephthalate (PET) and PTFE yarns, and the volume fraction of PTFE yarns in the braids; and

FIG. 3 is a plot representing a relationship between the initial bending rigidity of heterogeneous and homogeneous braids of PET and PTFE yarns, and the volume fraction of PTFE yarns in the braids.

DETAILED DESCRIPTION OF THE INVENTION

For purposes of describing this invention, a "heterogeneous" braid is a configuration composed of at least two sets of dissimilar yarns mechanically blended by intertwining the dissimilar yarns in a braided construction. The yarns are continuous and discrete, so therefore each yarn extends substantially along the entire length of the braid and maintains its individual integrity during braid preparation, processing and use.

The heterogeneous braids of this invention can be conventionally braided in a tubular sheath around a core of longitudinally extending yarns, although such a core may be excluded, if desired. Braided sheath sutures with central cores are shown in U.S. Pat. Nos. 3,187,752; 4,043,344; and 4,047,533, for example. A core may be advantageous because it can provide resistance to flattening, as well as increased strength. Alternatively, the braids of this invention can be woven in a spiral or spiroid braid, or a lattice braid, as described in U.S. Pat. Nos. 4,959,069 and 5,059,213.

The dissimilar yarns of the first and second set of yarns are braided in such a manner that at least one yarn from the first set is directly intertwined with, or entangled about, a yarn from the second set. Direct mechanical blending of individual, dissimilar yarns therefore occurs from the interweaving and interlocking of these dissimilar yarns, enhancing yarn compatibility and the overall physical and biological properties of the heterogeneous braid. Preferably, every yarn from the first set is in direct intertwining contact with a yarn of the second set to achieve the maximum degree of mechanical blending of the dissimilar yarns.

The first and second fiber-forming materials which make up the filaments of the first and second set of yarns, respectively, can be any materials capable of being spun into continuous filaments. Advantageously, the fiber-forming materials are nonmetallic.

The preferred fiber-forming materials are synthetic fiber-forming polymers which are melt or solution spun through a spinneret to prepare continuous filaments. The filaments so prepared are advantageously stretched to provide molecular orientation and annealed to enhance dimensional stability and/or biological performance. The fiber-forming polymers can be bioabsorbable or nonabsorbable, depending on the particular application desired. Examples of monomers from which bioabsorbable polymers are derived include, but are not limited to, some hydroxyacids and lactones, e.g. glycolic acid, lactic acid, glycolide, lactide, p-dioxanone, ϵ-caprolactone and trimethylene carbonate, as well as copolymers and polymer blends derived from these monomers and others. Interestingly, numerous bioabsorbable heterogeneous braids exhibiting varying useful biological properties, such as breaking strength retention in vivo and the absorption profiles in vivo, can be prepared for specific applications by using different combinations of bioabsorbable polymers.

Preferably, the continuous filaments which make up the first and second set of yarns are derived from nonabsorbable polymers. In a preferred embodiment, the first set of yarns acts as lubricating yarns to improve the overall pliability, or compliance, and surface lubricity of the heterogeneous braid. Preferably, the fiber-forming material of the first set exhibits a surface energy (which frequently relates to surface lubricity) less than about 38 dyne/cm, as measured by contact angle of liquids on polymer surfaces, as described by Kissa, E., "Handbook of Fiber Science and Technology," Vol. II, Part B, Marcel Decker, 1984. Such fiber forming polymers include perfluorinated polymers, e.g. PTFE and fluorinated ethylene/propylene copolymers (FEP) and perfluoroalkoxy (PFA) polymers, as well as non-perfluorinated polymers such as polyvinylidene fluoride (PVDF), polyethylene/tetrafluorethylene copolymers (PETFE), the polycholorofluoroethylene polymers, polypropylene (PP) and polyethylene (PE). More preferably, the first fiber-forming material exhibits a surface energy less than about 30 dyne/cm. The preferred polymers for the first set are PTFE, PETFE, FEP, PE and PP, and the most preferred fiber forming polymer is PTFE.

In a more preferred embodiment, the lubricating yarns of the first set are mechanically blended with yarns of the second set which act to provide improved strength to the heterogeneous braid. Preferably, the second set of yarns exhibits a yarn tenacity greater than 3.0 grams/denier, more preferably greater than 5.0 grams denier. The preferred yarns are PET, nylon and aramid, and the most preferred yarns are PET.

In the most preferred embodiment, the heterogeneous braid is composed of a first set of PTFE yarns mechanically blended with a second set of PET yarns in a braided configuration. Advantageously, the braided sheath encloses a core of longitudinally extending PET yarns to further improve the overall strength and resistance to flattening of the heterogeneous braid. In this embodiment, the volume fraction of lubricating yarns in the braided sheath and core desirably ranges from about 20 to about 80 percent. A volume fraction of lubricating yarns below about 20 percent will not typically improve the pliability of the braid, and a volume fraction above about 80 percent may adversely affect the overall strength of the braid. The filament fineness for such a heterogeneous braid is preferably less than 10 denier per filament, preferably from about 0.5 to about 5 denier per filament. A more coarse filament may result in a stiffer braid. The preferred individual yarn denier is between 10 and 100 denier.

The heterogeneous braids of this invention can be prepared using conventional braiding technology and equipment commonly used in the textile industry, and in the medical industry for preparing multifilament sutures. For example, the first and second set of yarns can be interwoven as indicated by the plan view of the yarn carrier layout of FIG. 1 for the preparation of a braided multifilament. The individual yarns of the braided sheath feed from spools mounted on carriers 22, 22' and

24, 24'. The carriers move around the closed circular loop 28, moving alternately inside and outside the loop 28 to form the braiding pattern. One or more carriers are continually following a serpentine path in a first direction around the loop, while the remaining carriers are following a serpentine path in the other direction.

In the illustrated embodiment, carriers 22, 22' are travelling around serpentine path 27 in a clockwise direction as indicated by directional arrows 23, and carriers 24, 24' are travelling around serpentine path 29 in a counterclockwise direction as indicated by arrows 25. The moving carriers dispense yarns which intertwine to form the braid. The yarns from all the carriers in a constructed embodiment of FIG. 1 are dispensed upward with respect to the plane of the drawing, and the braid is taken up on a reel located above the plane of the drawing.

In one embodiment, moving carriers 22, 24 dispense yarns of the first set and moving carriers 22', 24' dispense yarns of the second set to form the heterogeneous braid. In a more preferred embodiment, moving carriers 22, 22' dispense yarns of the first set and moving carriers 24, 24' dispense yarns of the second set. This carrier layout provides a braid in which each yarn of the first set is directly intertwined with a yarn from the second set.

Advantageously, as illustrated in FIG. 1, disposed within the center of the loop 28 are carriers 26 which dispense the core yarns of the braid. In the most preferred embodiment of this invention, moving carriers 22, 22' dispense PTFE yarns, moving carriers 24, 24' dispense PET yarns, and core carriers 26 dispense PET yarns.

Numerous additional embodiments are contemplated within the scope of the invention using conventional braiding technology and equipment. For example, the carrier layout can be modified to prepare a braid configuration using from 3 to 28 sheath carriers, with or without any number of core yarns. Dissimilar yarns from the first and second set of yarns can be plied together using conventional techniques before braiding, and in this embodiment, the carriers can dispense identical bobbins of plied yarns composed of individual yarns from the first and second sets. This embodiment not only offers the advantage of inter-yarn mechanical blending, but also the intimate mixing associated with intra-yarn blending.

Similar to the preparation of conventional homogeneous braids, the yarns from which the heterogeneous braids are prepared are preferably nontextured. The yarn tension during braiding is advantageously adjusted so that the yarn elongation for each set of yarns is about equal. The equilibration of yarn elongation may prevent irregularities, for example, "core popping", which is the tendency of core yarns to break through the braided sheath as the braid is bent. The number of picks per inch in the finished braid can be adjusted to balance the tensile strength of the braid with braid quality, e.g. the tendency for core popping and overall braid smoothness.

After the heterogeneous braid is prepared, it is desirably scoured to remove machine oils and lubricants, and any foreign particles. The scoured braid is preferably stretched at a temperature between the glass transition temperature and melting temperature of the lower melting set of yarns. Therefore, the stretching temperature is such that none of the yarns is actually melted. The stretching operation densifies the braid and improves braid smoothness. Afterwards, the braid may be annealed while under restraint to improve dimensional stability, and in the case of absorbable braids, to improve the breaking strength retention in vivo.

If desired, the surface of the heterogeneous multifilament braid can be coated with a bioabsorbable or nonabsorbable coating to further improve the handleability and knot tiedown performance of the braid. For example, the braid can be immersed in a solution of a desired coating polymer in an organic solvent, and then dried to remove the solvent. Most preferably, the coating does not cause the fibers or yarns to adhere to one another increasing stiffness. However, if the surface of the heterogeneous braid is engineered to possess a significant fraction of the lubricous yarn system, the conventional coating may be eliminated saving expense as well as avoiding the associated braid stiffening.

If the surface of the braid is coated, than the coating composition may desirably contain bioactive materials such as antibiotics and growth factors.

The post-treated heterogeneous braid is sterilized so it can be used for a host of medical applications, especially for use as a surgical suture, preferably attached to a needle. The braid can be sterilized using any of the conventional techniques well known in the art. For example, sterilization can be effected by exposing the braid to gamma radiation from a cobalt 60 source. Alternatively, the braid can be sterilized by exposure to ethylene oxide.

In the following examples, the tensile properties and knot security are each determined using an Instron Tensile Tester. The tensile properties, i.e. the straight and knot tensile strength and the percent elongation, are determined generally according to the procedures described in U.S. Pat. No. 4,838,267. The knot security, which provides an indication as to the number of throws required to secure a knot so that it fails to slip before cleanly breaking, is measured by first tieing a conventional square knot around a mandrel, pulling the knot apart on the Instron Tester to observe whether slipping occurs, and if so, then tieing knots with additional throws until 20 out of 20 knots break cleanly without slipping. The bending rigidity, which is the inverse of pliability, is determined using a Kawabata Pure Bending Tester, as discussed in "The Effects of Structure on the Geometric and Bending Properties of Small Diameter Braids", Drexel University Master Thesis, 1991, by Mr. E. Ritter.

The examples are illustrative only, and are not intended to limit the scope of the claimed invention. The types of yarns used to prepare the heterogeneous braid and the yarn geometry can be varied to prepare heterogeneous braids within the scope of the claimed invention which exhibit a combination of outstanding physical or biological properties.

EXAMPLES

Examples I and II describe heterogeneous braids of PTFE and PET yarns. In order to evaluate the relative performance of these braids, two controls are included which represent 100% PET and 100% PTFE braids, respectively. To the extent possible, the yarn materials and processing conditions are identical for the controls and heterogeneous braid examples. In addition, for comparison purposes, a braid is fabricated with identical materials but processed per the prior art U.S. Pat. No. 4,470,941.

CONTROL I

FIBER MATERIALS: An 8×0 PET braid is fabricated, i.e. 8 sheath yarns and 0 core yarns. All yarns are Dupont Dacron PET, 70 denier, 48 filament, type 52 yarn.

PROCESSING: The yarns are wound on braider bobbins per conventional methods, and the bobbins loaded on each carrier of a N.E. Butt 8 carrier braider. Machine settings include: 32 pick gear, 0.009" wire tension springs, and 183 rpm. The braid is aqueous scoured, and hot stretched at 30% draw ratio at 225° C.

CONTROL II

FIBER MATERIALS: An 8×0 PTFE braid is fabricated. All yarns are Dupont Teflon, 110 denier, 12 filament.

PROCESSING: The yarns are wound on braider bobbins per conventional methods, and the bobbins loaded on each carrier of a N.E. Butt 8 carrier braider. Machine settings include: 36 pick gear, no tension springs, and 183 rpm. The braid is scoured and hot stretched per the conditions described in CONTROL I.

EXAMPLE I

FIBER MATERIALS: An 8×0 heterogeneous braid is fabricated, consisting of four PET 70 denier yarns and four PTFE 110 denier yarns. The yarns are identical to that employed in CONTROL I and II. On a volume basis, the braid is 50.3% PET, and 49.7% PTFE.

PROCESSING: Four bobbins of PET yarn and four bobbins of PTFE yarn were wound by conventional means. The PET bobbins were loaded on the clockwise moving carriers of the N.E. Butt 8 carrier braider, and the PTFE yarn bobbins on the counter-clockwise moving carriers. Machine settings include: 32 pick gear, 0.009" tension springs on PET carriers, no springs on PTFE carriers, and 183 rpm. The braid is scoured and hot stretched per the conditions described in CONTROL I.

EXAMPLE II

FIBER MATERIALS: Identical to EXAMPLE I, except that 6 PET yarns and 2 PTFE yarns were used. On a volume basis, the braid is 75.5% PET, and 24.5% PTFE.

PROCESSING: Identical to EXAMPLE I, except that 2 PET bobbins replace 2 PTFE bobbins. All other braider machine settings, scour and hot-stretch conditions are identical to CONTROL I and II and EXAMPLE I.

PRIOR ART I

FIBER MATERIALS: Identical to EXAMPLE I. On a volume basis, the braid is 50.3% PET, and 49.7% PTFE.

PROCESSING: Identical to EXAMPLE I, except that the hot stretch temperature is at 300° C. and for a longer residence time to facilitate melting of the PET fibers.

The properties of CONTROLS I and II, and EXAMPLES I and II, and the PRIOR ART I are summarized in the following Table:

	USP DIAMETER (mils)	TENSILE STRENGTH (lbs)	KNOT STRENGTH (lbs)	BENDING RIGIDITY (gm × cm^2)	KNOT STABILITY (# of throws)
CONTROL I	10.68	4.98	3.14	0.0680	4
CONTROL II	9.11	2.58	2.04	0.0196	7
EXAMPLE I	9.71	3.55	2.41	0.0257	5
EXAMPLE II	10.35	4.10	2.67	0.0371	5
PRIOR ART I	8.81			0.0966	

As may be expected, the tensile strengths of the heterogenous braid examples reflect the relative contributions of the individual components. This behavior is said to follow the "rule of mixtures", i.e. the composite property is a weighted average of the component properties. In equation form,

$$P_c=(Vf_a)(P_a)+(Vf_b)(P_b)$$

where P_c is a composite property (such as tensile strength or modulus), P_a and P_b are the properties of the components a and b, and Vf_a and Vf_b are the volume fractions of components a and b. This behavior is clearly observed in FIG. 2, which shows a plot of tensile strength versus volume fraction of PTFE yarns for the Examples and Controls, in relation to the expected plot according to the rule of mixtures.

Surprisingly, the bending rigidity of the heterogeneous braids in EXAMPLES I and II do not follow the rule of mixtures, and show an enhanced bending rigidity relative to the weighted average of its components. This is shown in FIG. 3 as a plot of bending rigidity versus %PTFE in the braids. Bending rigidity is the inverse of pliability, and is obtained by measuring the slope of the *bending moment-radius of curvature* plot of a suture strand in pure bending. Hence lower bending rigidity relates to a more pliable suture, which is a highly desirable property. The mechanism of this enhanced pliability is believed to be internal lubrication of the braid by the "solid lubricant" behavior of the low surface energy PTFE.

U.S. Pat. No. 4,470,941 discloses the preparation of a "composite" suture with a monofilament-like surface made from multifilament yarns. The composite suture is composed of two different synthetic polymer fibers, which is thermally processed to melt one of the fibers to form a continuous matrix. This process was utilized to produce the PRIOR ART I example, the data of which is shown in Table 1 and FIG. 3. It is observed that the melting of the PET fibers significantly increases the braid bending rigidity due to the bonding of the "non-melted" fibers together, hence resulting in a less pliable braid of diminished utility.

What is claimed is:

1. A surgical suture consisting essentially of a heterogeneous braid composed of a first and second set of continuous and discrete yarns in a sterilized, braided construction wherein at least one yarn from the first set is in direct intertwining contact with a yarn from the second set; and

a) each yarn from the first set is composed of a plurality of filaments of a first fiber-forming material selected from the group consisting of PTFE, FEP, PFA, PVDF, PETFE, PP and PE; and

b) each yarn from the second set is composed of a plurality of filaments of a second fiber-forming material selected from the group consisting of PET, nylon and aramid; and

c) optionally a core.

2. The surgical suture of claim **1** wherein the suture is attached to a needle.

3. The surgical suture of claim **1** wherein the first fiber-forming material exhibits a surface energy less than about 38 dynes/cm.

4. The surgical suture of claim **3** wherein the first fiber-forming material exhibits a surface energy less than about 30 dynes/cm.

5. The surgical suture of claim **4** wherein the first set of yarns is PTFE.

6. The surgical suture of claim **5** wherein the second set of yarns exhibits a yarn tenacity greater than 3.0 grams/denier.

7. The surgical suture of claim **6** wherein the second set of yarns exhibits a yarn tenacity greater than 5.0 grams/denier.

8. The surgical suture of claim **1** wherein the second set of yarns is PET.

9. The surgical suture of claim **8** wherein the volume fraction of the first set of yarns in the braided sheath and core ranges from about 20 to about 80 percent.

10. The surgical suture of claim **9** wherein the fiber fineness of the yarns of the first and second sets is less than 10 denier per filament.

11. The surgical suture of claim **1** wherein at least one yarn from the first set of yarns is plied together to a yarn from the second set of yarns.

12. The surgical suture of claim **8** wherein the suture is attached to a needle.

* * * * *

EXHIBIT 5

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

C.A. NO. 04-12457 PBS

DePUY-MITEK, INC.,
A Massachusetts Corporation,
Plaintiff,
vs.
ARTHREX, INC.,
A Delaware Corporation,
Defendants.

CONFIDENTIAL - OUTSIDE COUNSELS' EYES ONLY

DAY 1 OF 2

DEPOSITION OF DR. DAVID S. BROOKSTEIN

Philadelphia, Pennsylvania

July 26, 2006

Reported by:

PAMELA HARRISON, RMR, CRR, CSR

see the deposition. I seem to recall he was also 02:52:38p
concerned about lubricity, but I don't -- I have 02:52:42p
to see the deposition. 02:52:45p
Q. That -- **02:52:46p**
A. That he wanted this to be a lubricious 02:52:49p
yarn. But I have -- I mean, UHMPE is known for 02:52:52p
its high lubricity. Okay. 02:52:56p
Q. I'm just trying to understand. I'm **02:52:59p**
just trying to understand, that ultra high -- the **02:53:02p**
ultra high molecular weight PE, that your **02:53:07p**
understanding -- you're relying upon Mr. Hallet's **02:53:10p**
testimony that it -- that the homogeneous braid **02:53:13p**
was constructed to get the strength of ultra high **02:53:17p**
molecular weight PE, is that correct? **02:53:20p**
A. That's what I wrote, but I'd like to 02:53:23p
see the deposition to see if there were other 02:53:24p
factors, that's what I'm saying. 02:53:26p
Q. Okay. Do you agree that ultra high **02:53:28p**
molecular weight PE adds strength to the braid -- **02:53:33p**
that a purpose of ultra high molecular weight PE **02:53:38p**
is to add strength to the braid? **02:53:41p**
A. It adds tensile strength but not 02:53:44p
holding strength. It actually detracts from knot 02:53:46p
holding strength. 02:53:50p
Q. But it adds tensile strength to the **02:53:50p**

braid? **02:53:53p**

A. It is my belief that it adds tensile strength to the braid. 02:53:53p 02:53:57p

Q. Okay. Now and then you write, and to get the flexibility of PET. What did you mean by that when you wrote that? What's your understanding? **02:53:57p 02:53:58p 02:54:01p 02:54:04p**

A. Well, ultra high molecular weight polyethylene, while it's very strong in tension, it is not very flexible. 02:54:06p 02:54:08p 02:54:13p

It also has other problems. People regularly mistake ultra high molecular weight polyethylene as being a strong fiber when in fact that's not the whole story, it's a bit silly. Ultra high molecular weight polyethylene is known very clearly for being very weak in compression and people make this mistake all the time. 02:54:16p 02:54:19p 02:54:21p 02:54:24p 02:54:26p 02:54:28p 02:54:31p 02:54:34p

Q. What do you mean by weak in compression? **02:54:35p**

A. We just -- we just gave you a -- a -- produced a paper that was given by a head scientist, Dyneema, where he specifically says it has poor axial compression properties. 02:54:37p 02:54:42p 02:54:44p 02:54:49p

Q. Well, what does that mean? I just -- **02:54:51p**

A. That means if you do any kind of 02:54:52p

BY MR. SABER: 09:41:32a

Q. Do you see, sir, in the paragraph beginning in Line 21 -- Line 31, a discussion of knot security? 09:41:32a 09:41:34a 09:41:38a

A. Yes, I do. 09:41:41a

Q. It begins on Line 36? 09:41:41a

A. I see that. 09:41:44a

Q. Do you see in the discussion of knot security is there any use of the word strength? 09:41:45a 09:41:47a

A. There's the word breaking, breaking the strength. 09:41:56a 09:41:58a

Q. I asked you if the word strength is there. 09:41:58a 09:42:00a

A. I do not see the word strength in there. 09:42:00a 09:42:02a

Q. Now, when the knot -- could you look at the column -- the chart between Columns 7 and 9? 09:42:03a 09:42:16a 09:42:24a

A. Yes. 09:42:24a

Q. Does the '446 patent use the word strength to describe the knot stability test? 09:42:26a 09:42:30a

MR. BONELLA: Wait. Now you've taken him to a chart. Now you've just asked him whether the patent describes. Are you saying the patent or the chart? 09:42:33a 09:42:37a 09:42:40a 09:42:40a

Q. All right. You have a sentence near the bottom of Page 15 -- 10:22:55a–10:22:59a

A. Page 15 or Paragraph -- 10:23:01a

Q. Page 15. Page 15. 10:23:02a

A. Page 15, oh, okay. 10:23:04a

Q. Right. Which is in Paragraph 27. 10:23:05a

A. That's not what you said, you said Paragraph 15 originally, but fine. 10:23:07a–10:23:09a

Q. Okay, I'm sorry. 10:23:10a

You say, In other words, the coating did not transform the braided FiberWire materials into another structure or cause it to lose its characteristics that are attributable to the dissimilar yarns being braided. 10:23:12a–10:23:27a

Do you see that sentence, sir? 10:23:29a

A. I see that sentence. 10:23:30a

Q. Is it your opinion that to affect the basic and novel characteristics of the invention as Dr. Mukherjee describes them, that the coating would have to transform the braided FiberWire materials into another structure or cause the braided FiberWire materials to lose its characteristics that are attributable to the dissimilar yarns being braided? 10:23:31a–10:23:58a

A. It is my opinion that if the coating in some miraculous way made those materials not yarns anymore and they were no -- they were not dissimilar anymore, that that would be a change. If all of a sudden what was once a set of two dissimilar yarns miraculously became, for instance, a monofilament, that would be a change, yeah. 10:24:09a 10:24:11a 10:24:15a 10:24:17a 10:24:22a 10:24:26a 10:24:29a 10:24:31a

Q. And that would affect the basic and novel characteristics? **10:24:32a 10:24:33a**

A. If the basic and novel characteristics are two dissimilar yarns, yes, and all of a sudden there weren't yarns in there anymore, it was some new material that was -- that we don't know about. 10:24:34a 10:24:35a 10:24:38a 10:24:41a 10:24:43a

Q. Or the yarns were the same yarns, made the yarns into the same yarns? **10:24:44a 10:24:46a**

A. If they were not dissimilar, right. 10:24:48a

Q. Right. So is it your opinion that if the coating does not -- does not achieve the goal that you just described, then it does not affect the basic and novel characteristics of the invention as Dr. Mukherjee defines it? **10:24:49a 10:24:54a 10:25:00a 10:25:02a 10:25:05a**

A. Can you repeat the question. 10:25:07a

Q. Yeah, let me try and rephrase it. **10:25:08a**

EXHIBIT 6

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. a Massachusetts Corporation Plaintiff, v. Arthrex, Inc. a Delaware Corporation Defendant.	Civil Action No. 04-12457 PBS

EXPERT REPORT OF DR. DEBI PRASAD MUKHERJEE
CONCERNING INVALIDITY OF U.S. PATENT NO. 5,314,446

Pursuant to the provisions of Rule 26(a)(2) of the Federal Rules of Civil Procedure, the Joint Case Management Statement adopted by the Court on February 18, 2005, and agreement between the parties, the undersigned, Dr. Debi Prasad Mukherjee, an expert witness for Defendants Arthrex, Inc. and Pearsalls, Limited (together, "Defendants") hereby sets forth his expert report as follows.

Linvatec's patent application no. 2004/0267313, covering its high-strength suture, just to name a few, all make clear that they are referring to UHMWPE. Such mention of UHMWPE is conspicuously absent from the '446 patent. Since UHMWPE is such a specialized material, and since there is no mention at all within the '446 patent of UHMWPE, it is my opinion that the '446 patent does not reasonably convey to a person of ordinary skill in the art at the time of the invention that the inventors were in possession of a sterilized surgical suture made at least in part with UHMWPE.

My opinion is further reinforced by what the '446 patent does disclose. For example, the '446 patent describes that the braid is made up of a first fiber-forming material mechanically interlocked or weaved with a second fiber-forming material. The materials described as first fiber-forming materials are PTFE, FEP, PFA, PVDF, PETFE, PP and PE. The materials described as second fiber-forming materials are PET, nylon and aramid.

The specification also states that the first fiber-forming materials are lubricious materials that act as lubricating yarns to improve the overall handling characteristics of the braid. The specification also explains that these lubricious materials are too weak to be used alone for most suture applications. The second fiber-forming materials are added to improve the overall strength of the braid. The '446 patent discloses that there is a tradeoff between the two fiber-forming materials – lubricious, but weak versus strong.

It is the very balance of lubricious yarns, which are good for handleability characteristics, with a strong yarn which is the hallmark of the patent specification. For example, the '446 patent relies heavily on what is called the "rule of mixtures" to attempt to demonstrate that this combination is an improvement in the art. But the point made by the inventors is that the gains in pliability and handleability by using the combination of lubricious, but weak materials with a stronger material outweighs the loss of suture strength resulting from combining a weaker lubricious material with the stronger material.

The '446 patent specification cautions against using more than about 80% of the lubricious yarns because such usage "may adversely affect the overall strength of the braid." This disclosure is also consistent with the tests described in the specification. For example, the Table depicts results for a multifilament braid made entirely (i.e., 100%) of a first fiber-forming material (i.e., CONTROL II made up of 100% PTFE). This braid was the weakest of the four braids tested, which is entirely consistent with the teachings of the specification.

These teachings of the '446 patent fairly describe the generally understood properties of general purpose PE – which is known to be lubricious, but weaker than the materials added for strength in the patent. Accordingly, the '446 patent specification would meet the "written description" requirement for general purpose PE. On the other hand, there is no written description of UHMWPE. Unlike general

purpose PE (or any of the other materials listed in the first fiber-forming group), UHMWPE is not a relatively weak material. Quite to the contrary, it is extremely strong and much stronger than any of the other materials identified in the first group of fiber-forming materials of claim 1. UHMWPE simply is not the kind of material which must be balanced against strong materials to achieve an acceptable suture. Moreover, for the reasons explained above, if the inventors had possession of UHMWPE as one of the first fiber-forming materials at the time of filing and believed that it met the teachings of the patent specification, I fully would have expected it to be specifically mentioned. The fact that it was not serves to reinforce my opinion that the inventors did not convey that they had possession of UHMWPE as a suture material at the time of the invention.

It is also my opinion that, viewed from the perspective of a person skilled in the art in February 1992, the '446 patent does not teach such a person how to make and use a surgical suture including UHMWPE without having to resort to undue experimentation.

As described above, nowhere does the '446 patent specification mention that UHMWPE can be used in the disclosed braided sutures. The entirety of the disclosure of the first fiber-forming materials in consistent with general purposes PE and inconsistent with UHMWPE. As described above, UHMWPE is a highly specialized material that also has very different properties as compared with every other material included in the '446 patent specification. The specification describes a manner of

Dated: March 3, 2006

Debi Prasad Mukherjee

Debi Prasad Mukherjee, Sc. D.

EXHIBIT 7

DePuy Mitek's Privileged Document List
Civil Action No. 04-12457 PBS

January 25, 2006

Tab	Date	Document	Author	Recipient	Privilege Claimed	Description
1	09/20/02	Presentation			Attorney-Client	DMI001096A and DMI001098A: Redacted portions relate to legal advice concerning patent searches and results
2	11/21/03	Presentation			Attorney-Client	DMI001015A: Redacted portion relates to legal advice concerning patent searches and results
3	05/22/03	Presentation	George Cook		Attorney-Client	DMI001068A, DMI001070A, DMI001071: Redacted portions relate to legal advice concerning assessment of issued patents.
4	11/21/03	Presentation	Unknown		Attorney-Client	DMI001041A: Duplicate of privileged document #2
5	05/22/03	Presentation	George		Attorney-Client	DMI001083A, DMI001089, DMI001090A: Redacted portions relates to legal advice concerning issued patents
6	05/22/03	Presentation	George		Attorney-Client	DMI000981, DMI000984, DMI000992A: Redacted portions relate to legal advice concerning impact of issued patents
7	11/25/03	Presentation	McAlister Cook		Attorney-Client	DMI000973 and DMI000976: Redacted portions relate to legal advice concerning impact of issued patents
8	05/14/04	Report	Seppa		Attorney-Client	DMI000455: Redacted portion relates to legal advice concerning issued patents
9	09/23/97	Letter	Groening*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
10	10/20/97	Letter	Woodrow*	Groening*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
11	09/23/97	Letter with handwritten notes	Groening*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
12	09/23/97	Letter with handwritten notes	Groening*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
13	09/23/97	Letter with handwritten notes	Groening*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
14	06/07/96	Letter	Groening*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
15	01/22/96	Letter	Woodrow*	Fritzsche*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
16	12/05/95	Letter	Fritzsche*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application

Tab	Date	Document	Author	Recipient	Privilege Claimed	Description
17	07/08/93	Memo with notes	Clickner	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning German Hunter patent application
18	07/22/02	Letter	Yasuda*	Wissing*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
19	07/17/01	Letter	Wissing*	Yasuda*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
20	07/17/01	Letter with notes	Wissing*	Yasuda*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
21	04/27/01	Letter	Yasuda*	Weiss*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
22	04/26/01	Letter	Yasuda*	Woodrow*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
23	04/02/03	Letter	Yasuda*	Wissing*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
24	06/25/03	Letter	Yasuda*	Loo*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
25	06/13/03	Letter with notes	Loo*	Odajima*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
26	06/13/03	Email	Palko*	Odajima*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
27	06/11/03 06/11/03	Email Email	Loo* Loo*	Odajima* Palko*	Attorney-Client Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
28	06/11/03	Email	Loo*	Odajima*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
29	04/02/03	Letter	Yasuda*	Wissing*	Attorney-Client	Communication reflecting legal advice concerning Japanese Hunter patent application
30	06/21/04	Report	Burkley	Seppa Howe	Attorney-Client/ Work Product	Communication seeking legal advice regarding patent infringement and reflecting work preformed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
31	Undated	Draft Invention Disclosure	Koyfman Brucker Hill		Attorney-Client	Communication to counsel seeking legal advice concerning patentability of invention
32	07/15/04	Memo	Seppa	Skula* McAlister Leibowitz	Attorney-Client/ Work Product	Communication to counsel seeking legal advice concerning patent infringement and reflecting work preformed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.

*=Attorney/Paralegal/Patent Agent

Tab	Date	Document	Author	Recipient	Privilege Claimed	Description
33	08/19/04	Memo	Seppa	Skula* McAlister Leibowitz	Attorney-Client/ Work Product	Communication to counsel seeking legal advice concerning patent infringement and reflecting work preformed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
34	02/18/04	Report	Seppa	Distribution	Attorney-Client/Work Product	Communication to counsel seeking legal advice concerning patent infringement and reflecting work preformed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
35	11/25/03	Presentation	McAlister Cook		Attorney-Client	DMI006571: Redacted portion relates to legal advice concerning issued patents
36	11/08/02	Report	Longstreet	Ethicon GMB	Attorney-Client	DMI038171: Redacted portion relates to communication seeking legal advice concerning the patentability of an invention.
37	08/07/03	Plan			Attorney-Client	DMI039134: Redacted portion relates to reflecting legal advice concerning third party patent rights
38	Undated	Presentation			Attorney-Client	DMI0039239: Redacted portion relates to legal advice concerning Orthocord patent claims
39	Undated	Presentation			Attorney-Client	DMI39400: Redacted portion relates to request for legal advice concerning issued patents
40	09/02/03	Report	Koyfman Pokropinski		Attorney-Client	DMI039422: Redacted portion reflects legal advice concerning scope of issued patents
41	09/24/03	Report	Koyfman Pokropinski		Attorney-Client	DMI039447: Redacted portion reflects legal advice concerning scope of issued patents
42	11/04/02	Report	Dormier		Attorney-Client	DMI039473, DMI039474, DMI039475, DMI039486 and DMI039490: Redacted portions reflects legal advice concerning scope of issued patents
43	11/05/01	Report	Longstreet		Attorney-Client	DMI039496-97: Redacted portions reflects legal advice concerning scope of pending patent applications
44	02/27/03	Presentation			Attorney-Client	DMI039501, DMI039508 and DMI039513: Redacted portions reflect legal advice concerning issued patents and freedom to operate
45	09/02/04	Outline	Seppa		Attorney-Client/ Work Product	DMI039518: Redacted portion reflects legal advice and work performed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
46	Undated	Notes			Attorney-Client	DMI039558: Redacted portion relates to reflects legal advice concerning issued patents

*=Attorney/Paralegal/Patent Agent

Tab	Date	Document	Author	Recipient	Privilege Claimed	Description
47	07/26/04	Outline			Attorney-Client/ Work Product	DMI039560: Redacted portion reflects legal advice and work performed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
48	06/29/04	Outline			Attorney-Client/ Work Product	DMI039571: Redacted portion reflects legal advice and work performed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
49	07/28/03	Report	Koyfman		Attorney-Client	DMI039621: Redacted portion reflects legal advice concerning issued patents
50	04/13/04	Presentation			Attorney-Client/ Work Product	DMI039675 and DMI039678: Redacted portion reflects legal advice concerning issued patents and pending patent application and reflects work performed at the direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
51	09/26/03	Report	Nozad		Attorney-Client	DMI039707: Redacted portion reflects request for legal advice concerning pending patent third party applications
52	Undated	Presentation			Attorney-Client	DMI039726 and DMI039747: Redacted portions relate legal advice concerning pending patent application and analysis of third party patent rights
53	Undated	Presentation			Attorney-Client	DMI039759: Redacted portions relate to legal advice concerning analysis of third party patent rights
54	5/27/04	Report	Seppa	Distribution	Attorney-Client/Work Product	Communication to counsel seeking legal advice concerning patent infringement and reflecting work preformed at direction of counsel in anticipation of patent litigation with Arthrex concerning the Hunter patent.
55	Undated	Filed Application with handwritten notes	Matthew Goodwin*		Attorney Client	Notes reflect Examiner's comments and proposed amendments and attorney analysis of the same in furtherance of providing legal advice concerning patentability of invention
56	12/2/91	Letter	Matthew Goodwin*	M. Steckel	Attorney-Client	Communication reflecting legal advice concerning patent application
57	7/26/93	Letter	Dennis Jamiolkowski	Hal Woodrow* Donald Regina	Attorney-Client	Communication to counsel in furtherance of providing legal advice concerning response to Office Action from the USPTO
58	8/3/92	Letter	A. Hunter	Matthew Goodwin*	Attorney-Client	Communication to counsel in furtherance of providing legal advice concerning a response to an Office Action from the USPTO

*=Attorney/Paralegal/Patent Agent

Tab	Date	Document	Author	Recipient	Privilege Claimed	Description
59	12/20/91	Letter	Charles Fritz	Matthew Goodwin* M. Steckel	Attorney-Client	Communication to counsel seeking legal advice concerning the patentability of invention
60	6/4/91	Letter	Matthew Goodwin*	M. Steckel	Attorney-Client	Communication from counsel reflecting legal advice concerning the patentability of invention
61	11/18/91	Letter	Mark Steckel	Matthew Goodwin* A. Finkenaur R. Lilenfeld B. Schwartz A. Skinner	Attorney-Client	Communication to counsel seeking legal advice concerning the patentability of invention
62	7/14/92	Letter	Matthew Goodwin*	A. Hunter D. Jamiolkowski	Attorney-Client	Communication from counsel seeking information in connection with rendering legal advice concerning a response to an Office Action from the USPTO
63	11/20/92	Letter	A. Hunter	Matthew Goodwin*	Attorney-Client	Communication to counsel seeking legal advice concerning the patentability of invention
64	11/13/92	Letter with handwritten comments	Matthew Goodwin*	Al Hunter Dennis Jamiolkoski	Attonrey-Client	Communication from counsel in connection with providing legal advice concerning the patentability of invention and handwritten notes reflecting conversations concerning patentability of invention
65	11/15/93	Letter to File	Hal Woodrow*	File	Attorney-Client	Communication from counsel reflecting legal advice concerning analysis of Examiner's amendment and inventorship issues
66	Undated	Filed Application with handwritten notes	Hal Woodrow*		Attorney-Client	Notes reflect Examiner's comments and proposed amendments and attorney analysis of the same in furtherance of providing legal advice concerning patentability of invention
67	Undated	Filed Application with handwritten notes	Matthew Goodwin*		Attorney-Client	Notes reflect Examiner's comments and proposed amendments and attorney analysis of the same in furtherance of providing legal advice concerning patentability of invention
68	Undated	Letter to File	Hal Woodrow*	File	Attorney-Client	Communication from counsel reflecting legal advice concerning analysis of art cited abroad
69	1/8/90	Invention Disclosure Memorandum	Mark Steckel	Dr. C. Fritz Mr. A. Hunter Mr. D. Jamiolkowski Mr. D. Rembert Dr. B. Schwartz Dr. A. Skinner	Attorney-Client	Communication forwarded to counsel seeking legal advice concerning the patentability of invention

*=Attorney/Paralegal/Patent Agent

EXHIBIT 8

United States Patent [19]

Capozza

[11] **4,074,713**

[45] **Feb. 21, 1978**

[54] **POLY(N-ACETYL-D-GLUCOSAMINE) PRODUCTS**

[75] Inventor: **Richard Carl Capozza**, Norwalk, Conn.

[73] Assignee: **American Cyanamid Company**, Stamford, Conn.

[21] Appl. No.: **707,914**

[22] Filed: **July 22, 1976**

Related U.S. Application Data

[62] Division of Ser. No. 558,525, March 14, 1975, Pat. No. 3,989,535, which is a division of Ser. No. 441,717, Feb. 11, 1974, abandoned.

[51] **Int. Cl.**[2] **A61F 5/04**

[52] **U.S. Cl.** ..... **128/92 C**

[58] **Field of Search** ..... 3/1; 128/92 C; 424/180

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,605,123	9/1971	Hahn	3/1
3,632,754	1/1972	Balassa	424/180
3,878,284	4/1975	Schmitt et al.	260/33.4 R
3,879,377	4/1975	Austin	424/180
3,892,731	7/1975	Austin	424/180
3,903,268	9/1975	Balassa	424/180
3,914,413	10/1975	Balassa	424/180

Primary Examiner—Leland A. Sebastian

Attorney, Agent, or Firm—Charles F. Costello, Jr.

[57] **ABSTRACT**

Poly(N-acetyl-D-glucosamine) is soluble in hexafluoroisopropyl alcohol and hexafluoracetone sesquihydrate. The solutions formed may be wet or dry spun into filaments, or cast into films or solid articles, which may be used as absorbable surgical sutures, or other absorbable surgical elements. Poly(N-acetyl-D-glucosamine) is enzymatically degradable in living tissue, and is resistant to hydrolytic degradation, and, therefore, surgical elements thereof have good storage characteristics under a wide variety of conditions.

2 Claims, No Drawings

POLY(N-ACETYL-D-GLUCOSAMINE) PRODUCTS

This is a division of application Ser. No. 558,525, filed Mar. 14, 1975, now U.S. Pat. No. 3,989,535, which is a division of application Ser. No. 441,717, filed Feb. 11, 1974, now abandoned. Another division of said Ser. No. 441,717 is application Ser. No. 558,526, filed Mar. 14, 1975, U.S. Pat. No. 3,988,411.

BACKGROUND OF THE INVENTION

Poly(N-acetyl-D-glucosamine) is a known polymer which is a component of naturally occurring chitin. It is regarded as insoluble in conventional solvents, and, therefore, has been used as a powder. There is a demand for absorbable surgical elements, particularly sutures, which are strong enough of serve as a tissue retaining element during a healing process, and which then are absorbed by the living tissue. Requirements for the duration of useful strength vary widely with both the type of tissue and the surgical procedure. Some cosmetic purposes require strength for only a few hours or a few days. Other uses require strength for periods of months or even years. Advantageously, the surgical element should absorb promptly after it has served its useful function. Sutures have long been treated with dyes and therapeutic agents, poly(N-acetyl-D-glucosamine) sutures may be so treated.

Absorbable surgical elements usually start losing strength almost as soon as implanted, but a useful degree of strength is maintained for a much longer period. Complete absorption is, of course, much slower. Sharp changes in strength with time are not to be expected.

DESCRIPTION OF THE PRIOR ART

U.S. Pat. No. 3,297,033, Schmitt and Polistina, January 10, 1967, SURGICAL SUTURES, discloses polyhydroxyacetic ester absorbable sutures. The material is also called polyglycolic acid, and is disclosed as permitting small quantities of comonomers to be present, such as dl-lactic acid, its optically active forms, homologs and analogs. A small quantity is recognized by the art as up to 15%, as shown by U.S. Pat. No. 2,668,162, Lowe, Feb. 2, 1954, PREPARATION OF HIGH MOLECULAR WEIGHT POLYHYDROXYACETIC ESTER.

Many uses of polyglycolic acid for surgical purposes are disclosed in said U.S. Pat. No. 3,297,033 and continuations-in-part thereof including: U.S. Pat No. 3,463,158, Schmitt and Polistina, Aug. 26, 1969, POLYGLYCOLIC ACID PROSTHETIC DEVICES; U.S. Pat. No. 3,620,218, Schmitt and Polistina, Nov. 16, 1971, CYLINDRICAL PROSTHETIC DEVICES OF POLYGOLYCOLIC ACID; U.S. Pat. No. 3,739,773, Schmitt and Polistina, June 19, 1973, POLYGLYCOLIC PROSTHETIC DEVICES; and U.S. Ser. No. 365,656, Schmitt and Polistina, May 31, 1973, SURGICAL DRESSINGS OF ABSORBABLE POLYMERS.

U.S. Pat. No. 3,463,158, Schmitt and Polistina, Aug. 26, 1969, POLYGLYCOLIC ACID PROSTHETIC DEVICES, discloses surgical uses of polyglycolic acid, and incorporates definitions of some terms.

U.S. Pat. No. 3,620,218, Schmitt and Polistina, Nov. 16, 1971, CYLINDRICAL PROSTHETIC DEVICES OF POLYGLYCOLIC ACID, lists many surgical uses of polyglycolic acid.

u.S. Pat. No. 3,737,440, Schmitt and Bailey, June 5, 1973, POLYGLYCOLIC ACIDS IN SOLUTIONS,

discloses hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate as solvents for the preparation of solutions of polyglycolic acid, and wet and dry casting of such solutions. Polyglycolic acid has many surgical uses as an absorbable to polymer.

Polyglycolic acid sutures are the only synthetic absorbable sutures that have met with commercial surgical acceptance to date.

Chitin has been estimated to be the second most abundant polysaccharide in nature with a synthesis in the neighborhood of a billion tons a year by marine organisms. See Chitin, N. V. Tracey, Reviews of Pure and Applied Chemistry, Royal Australian Chemical Institute, Vol. 7, No. 1, March, 1957, pages 1 to 14.

Carboxymethylchitin is disclosed in Carbohyd, Res. 7, 483-485 (1968), Ralph Trujillo.

This article mentions the hydrolysis of both chitin and carboxymethylchitin by lysozyme.

I. Joffe and J. R. Hepburn, "Observations on Regenerated Chitin Films", J. Materials Science, 8 (1973), 1751-1754, give values on the strength of films of regenerated chitin, from a chitin xanthate disperson — including a comparison of strength after 30 years storage. Values as high as $9.31 \times 10^7 Nm^{-2}$ are given (calculates to 6.3×10^3 pounds/sq. inch).

Noguchi, Wada, Seo, Tokura and Nishi, "Studies on Chitin and Chitin-Cellulose Fibers", Kobunshi Kagaku, Vol. 30, No. 338, pp. 320-326 and 378, (June 1973) disclose chitin fibers spun by a xanthate processs, analogous to the spinning of cellulose to form rayon. A 50% chitin-cellulose fiber is disclosed with a denier of 12.3 and a tenacity of 1.08 grams/denier dry and 0.13 grams/denier wet.

Poly(N-acetyl-D-glucosamine) differes from cellulose in that instead of a hydroxyl group in the 2 position on cellulose, there is an acetylamino group.

Prudden, Migel, Hanson, Freidrich and Balassa in "The Discovery of a Potent Pure Chemical Wound-Healing Accelerator", The American Journal of Surgery, Vol. 119, May 1970, pages 560 to 564, disclose that chitin containing n-acetyl glucosamine is useful to accelerate wound-healing. These authors postulate fibers of a long chain n-acetyl glucosamine as a nonabsorbable suture, and a shorter polymer length as an absorbable suture. Other prosthetic devices, such as hemostatic clips, vascular and joint protheses, mesh and knit abdominal thoracic wall replacements are postulated for evaluation. No methods are postulated for the achievements of these objectives. incorporated by this reference thereto for background information on chitin, its properties and derivatives.

SUMMARY OF THE INVENTION

This invention relates to solid surgical elements of poly(N-acetyl-D-glucosamine), methods of making them, and more particularly to polymers which are compatible with living mammalian tissue, particularly human tissue, and which can be used surgically, and are biologically degradable into tissue compatible components which are absorbed by living tissues. The primary degradation of the polymer is by enzymatic fission into products which can be carried away by the living tissue and which products are degradable to excretable components or are themselves excretable. Because of the surgical demand for sutures, absorbable fabrics, gauzes, bone pins, etc. whose absorption and strength characteristics vary, it is desirable that a spectrum of strength and absorbability characteritstics be provided to meet

surgical demands for various procedures. The enzyme lysozyme is particularly effective in the enzymatic degradation of poly(N-acetyl-D-glucosamine). Various forms of poly(N-acetyl-D-glucosamine) may have different degradation rates, and the degradation rate may vary with the location.

Poly(N-acetyl-D-glucosamin) has many advantages as a material of construction for sutures and other surgical elements. The poly(N-acetyl-D-glucosamine) in its own right tends to encourage wound healing rather than slow it down. Poly(N-acetyl-D-glucosamine) is biodegradable by enzymatic action with minimal tissue reaction.

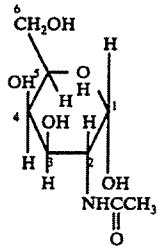
Surgical elements of poly(N-acetyl-D-glucosamine) are not hydrolyzed by water and, hence, need not be kept bone dry but may be stored under ambient comditions of moisture for prolonging periods of time. The basic poly(N-acetyl-D-glucosamine) may be modified by treatment to introduce carboxymethyl, hydroxyethyl or O-ethyl substituents so that the polymer has linkages from acetyl-6-O-(carboxymethyl)-D-glucosamine units, acetyl-6-O-(2'-hydroxyethyl)-D-glucosamine units, or acetyl-6-O-(ethyl)-D-glucosamine units. Since modification by the introduction of these derivatives alters the rate of enzymatic degradation, such inroduction provides a means for controlling the absorption rate as well as making the surgical element more hydrophilic or more hydrophobic to an extent desired.

Other side chains may be placed on the glucosamine ring, or its substituents because the side chains may vary from methyl to long chain alkyl, including branched chains, unsaturated chains, aryl or aralkyl, and which may include halogen, alkoxy, aryloxy, aralkoxy, ether, ester and amide groups, as substituents on the side chains, the relative distribution between aqueous and solvent components in a system can be varied as well as water solubility or oil and solvent solubility. Also, because the size and location of the side chains affects the rate of degradation and the acidity of the system, the rate of enzymatic degradation can be varied over wide limits to meet the requirements of a system and the desires of the operator. The less highly substituted materials are often preferred for medical uses. The broader range of substituents permits more flexibility in pH control, and in biodegradable polymers for use in packaging, etc. The use of side chains with unsaturated linkages permits cross-linked polymers to be formed. This uniformity results in greater strength, more crystallinity, and more readily reproducible andcontrollable characteristics, which are of interest to a surgeon during use.

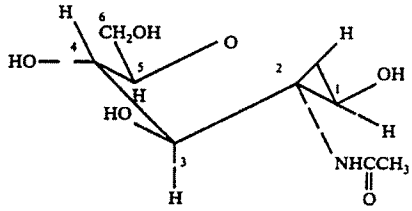
Fibers made by extruding solutions of poly(N-acetyl-D-glucosamine) in polyfluorinated solvents such as hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate or mixtures of such solvents permit dry or wet spinning of fibers which are of a convenient size for forming sutures.

The fibers are more pliable when wet with water. The enhanced pliability, when wet with water, is highly advantageous in that many surgeons are accustomed to handling catgut which must be wet with water to have adequate handleability and, hence, are using familiar techniques snd procedures in surgery. Monofilaments are usable when wet. A dry braided construction of polyfilamentary character is frequently advantageous.

Poly(N-acetyl-D-glucosamine) has the formula:

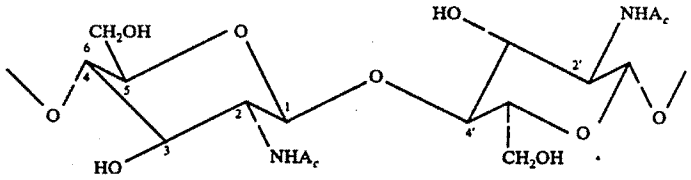


or



Groups below the plane of the paper are shown by a dotted bond.

Poly(N-acetyl-D-glucosamin) has ascribed to it the formula (ring hydrogens omitted for clarity):



Poly(N-acetyl-D-glucosamine) is a major component of naturally occurring chitin. The naturally occuring material has not only the poly(N-acetyl-D-glucosamine) but also inorganic salts thought to be forms of calcium carbonate and proteinaceous material, the composition of which is not presently known. The term "chitin" is used herein to refer to the various naturally occurring forms of chitin including the protein and inorganic carbonate components. The term "purified" is used to refer to chitin after purification to remove calcium carbonate and other inorganic salts and various proteins which may be present and is essentially poly(N-acetyl-D-glucosamine). Some confusion exists in the literature in that the name chitin is used as a name for poly(N-acetyl-D-glucosamine) wihtout specifying whether it is a naturally occurring material containing inorganic salts and proteings or whether the term is intended to designate purified poly(N-acetyl-D-glucosamine) without specifying the degree of purity or the character of the impurities present.

The term "drug" is used to refer to a substance other than a food intended to affect the structure or function of the body of man or other animal. The term is somewhat broader than "medicine" in that the term "medicine" is sometimes considered to be restricted to an

agent which is administered to affect or control a pathogenic condition.

The term "enzymatically degradable" refers to a form of poly(N-acetyl-D-glucosamine) or its derivatives which is broken down into body fluid soluble components. The problem of retention by the body or disposal of the residual matrix is minimal or non-existent.

While other enzymes may also affect the enzymatic degradation of the poly(N-acetyl-D-glucosamine) matrix, the enzyme which is most widely distributed in the body and here very effective is lysozyme. Lysozyme occurs in practically all of the body fluids and effectively breaks down the polymer chain to water soluble or disposable components.

Poly(N-acetyl-D-glucosamine) is not readily hydrolyzed by water.

It is highly advantageous to have the degradation of the poly(N-acetyl-D-glucosamine) occur only by the action of an enzyme as the resistance to hydrolytic degradation markedly reduces problems of manufacture and storage in the presence of ambient moisture, and ensures a steady smooth surface erosion rather than a fragmentation process commonly experience by polymers which are hydrolyzed by small molecules.

The degradation rate of poly(N-acetyl-D-glucosamine) can be lowered by crosslinking, if a slower rate is preferred.

In general, the surgical uses of the polymers of the present invention are similar to those previously taught for polyglycolic acid and as set forth in U.S. Pat. Nos. 3,297,033; 3,463,158; 3,620,218; and 3,739,773, and U.S. Ser. No. 365,656, supra. These disclosures of uses as herein hereby incorporated by this reference thereto.

These uses are extremely varied. For clarity and explanation, certain terms are defined and representative uses given for the novel polymer forms.

A "filament" is a single, long, thin flexible structure of a non-absorbable or absorbable material. It may be continuous or staple.

"Staple" is used to designate a group of shorter filaments which are usually twisted together to form a longer continuous thread.

An absorbable filament is one which is absorbed, that is, digested or dissolved, in living mammalian tissue.

A "thread" is a plurality of filaments, either continuous or staple, twisted together.

A "strand" is a plurality of filaments or threads twisted, plaited, braided, or laid parallel to form a unit for further construction into a fabric, or used per se, or a monofilament of such size as to be woven or used independently.

A "fabric" is a three dimensional assembly of filaments, which may be woven, knitted, felted or otherwise formed into a flexible sheet having two layer dimensions and a thinner thickness dimension. A fabric may be cut to a desired size before or at the time of use.

Except where limited specifically or by context, the word fabric includes both absorbable and non-absorbable cloth, or a fabric or cloth that is partially of absorbable polymer.

A "dressing" is a woven, knitted, felted or braided fabric, of at least one layer, which is designed to protect a wound and favor its healing. As used herein, the term dressing includes bandages, insofar as they contact the wound itself. The dressing may be entirely internal.

A "bandage" is a strip of gauze, or other material used to hold a dressing in place, to apply pressure, to immobilize a part, to obliterate tissue cavities or to check hemorrhage. Except insofar as the bandage comes in contact with a wound, or the exudate from a wound, there is no need for the bandage to be of absorbable polymer. If the bandage may be in a position where absorbability by living tissue of at least part of the bandage is desirable, at least that part should be of absorbable polymer.

The dresing may be in part directive of growth, as, for example, in nerve tissue, which grows slowly, and as a result has regeneration impaired by the more rapid growth of scar tissue which can block the growth of the nerve tissue. With a wrap-around sheath of absorbable polymer fabric or a split or solid tube used to support, place, hold and protect; regeneration of nerve tissue and function is greatly aided. Other factors may inhibit regeneration of nerve tissue or function, but with the exclusion of scar tissue, such other factors may be separately treated.

For different purposes and in different types of tissue the rate of absorption may vary. In general, an absorbable suture or solid load bearing prosthesis should have as high a portion of its original strength as possible for at least three days, and sometimes as much as thirty days or more, and preferably should be completely absorbed by muscular tissue within from 45 to 90 days or more depending on the mass of the cross-section. The rate of absorption in other tissues may vary even more.

For dressings, strength is often a minimal requirement. Some dressings, as for instance, on a skin abrasion, may need strength for only a few hours, until a scab forms, and rapid decrease of strength and absorption is an advantage so that when the scab is ready to fall off, the dressing does not cause a delay. For burns, and larger lesions, strength and reinforcement may be desired for a longer period.

In common with many biological systems, the requirements are not absolute and the rate of absorption as well as the short-term strength requirement varies from patient to patient and at different locations within the body, as well as with the thickness of the section of the polymer.

The absorbably polymer may be formed as tubes or sheets for surgical repair and may also be spun as thin filaments and woven or felted to form absorbable sponges or absorbable gauze, or used in conjunction with other compressive structures as prosthetic devices within the body of a human or animal where it is desirable that the structure have short-term strength, but be absorbable. The useful embodiments include tubes, including branched tubes or Tees, for artery, vein or intestinal repair, nerve splicing, tendon splicing, sheets for typing up and supporting damaged kidney, liver and other intestinal organs, protecting damaged surface areas such as abrasions, particularly major abrasions, or areas where the skin and underlying tissues are damaged or surgically removed.

In surgical techniques involving internal organs, hemorrhage may be a major problem. Some of the organs have such tissue characteristics that it is very difficult to use sutures or ligatures to prevent bleeding. For example, the human liver may suffer traumatic damage or exhibit tumors or for other reasons require surgery. In the past it has been very difficult to excise part of the liver or to suture the liver without the combined problems of the sutures cutting out and hemorrhage at the surface causing such major complications as to either prevent surgery or cause an unfavorable prognosis.

It is now found that a sponge or pad or velour of the present absorbable polymer may be used to protect the surface and permit new feats of surgical intervention. For instance, filaments may be formed into a woven gauzwe or felted sponge or a velour, preferably the construction is fairly tight by textile standards, and such sponge may be placed on the surface of the bleeding organ such as the liver or a lung with either gentle suturing or with ties in the nature of ligatures to hold the element in position with a certain amount of body fluids flowing into the sponge and being absorbed, which results in hemostasis and prevention of further loss of body fluids. If a liver or lung is so repaired, the organ may be replaced in the body cavity and the wound closed.

Where surgically useful, the sponge or fabric can be used as a bolster to prevent a suture from cutting out. For instance, if the liver is to be sutured, an absorbable polymer pad can be placed on the surfaces to reinforce the tissue and prevent the suture from cutting into rather than retaining the tissue. Such pads of gauze or felt protect tissue from cutting.

Absorbable pads, bandages or sponges are extremely useful in surgical techniques in which it is the intent to remove the major portion or all of such sponges, felt or pads but, through inadvertence or accident, part of it may remain. For instance, in a surgical operation one of the problems which arises is the lint from cotton sponges remaining in the wound. If absorbable polymer sponges are used, any small fragments which are addicentally displaed are absorbed without incident and even if a sponge is left in the wound, the deleterious effects are minimal.

The use of a synthetic absorbable polymer as a sponge or pad is particularly advantageous for surface abrasions. In the past it has been necessary to put on a dressing and avoid having the non-absorbable dressing grow into the tissue at all costs. If elements of an absorbable polymer gauze are beneath the regenerating tissue level, the tissue will regenerate and absorb the polymer with the residual polymer in the scab falling off when the scab is displaced.

The dressing that contacts tissue should be sterile. A strippable sterile package is a convenient storage system to maintain sterility between the time of manufacture and time of use.

Even in cosmetic surgery or skin surgery, where in the past it has been quite customary to use silk sutures and, after the tissue is regenerated sufficient to be self-retaining, remove the sutures so that they do not leave scars, the use of synthetic absorbable polymer sutures now permits implantaton of sutures through the skin with the part below the skin surface being absorbed and the part above the skin surface falling off. The resulting minimal degree of scarring at the skin surface is highly advantageous.

In surgery various tissues need to be retained in position during healing. Defects and wounds of the abdominal wall, chest wall and other such tissues need to be reconstructed. For a hernia, a permanent slice or reinforcement is often desired as shown in Usher, U.S. Pat. No. 3,054,406, SURGICAL MESH, or U.S. Pat. No. 3,124,136, METHOD OF REPAIRING BODY TISSUE. For some surgical procedures, a temporary reinforcing is desired to provide strength while body tissues are healing; and after the body tissues have assumed the load, foreign components are no longer desired. Tissue retention using the general techniques disclosed in the Usher patents, supra, are readily accomplished using either an absorbable synthetic polymer monofilament or polyfilament fabric or mesh or by using a non-absorbable material such as polyethylene or polypropylene or polyester woven as a bicomponent mesh or kit with an absorbable synthetic polymer. The use of a bicomponent fabric has the advantage of giving additional early strength for holding the tissues in position during initial regeneration with the absorbable portions being absorbed, thus permitting body tissues to invade and reinforce the permanent mesh.

In common with other surgical procedures, it is often desirable that a bicomponent structure be used which provides the spacing desired for non-absorbable elements, with the absorbable synthetic polymer element holding the structure in a desired geometrical configuration at the start of the healing process. As the element is absorbed, regenerating tissue invades and replaces the dissolved synthetic polymer so that the non-absorbed element is left in a desired configuration, interlaced with living tissue in a stress-transferring relationship.

The choice of non-absorbable reinforcement, a partially absorbable reinforcement, or a completely absorbable reinforcement is a matter of surgical judgment, based upon the condition of the patient, the body structure under treatment, and other medical factors.

For instance, a synthetic absorbable polymer sponge may be used in a cavity after tooth extraction to stanch the flow of blood. The sponge is either absorbed by regenerating tissue, or disintegrates into the mouth, permitting improved recovery after extractions.

The medical uses of the polymers of the present invention include, but are not necessarily limited to:

A. Absorbable polymer alone

1. Solid Products, molded or machined
   a. Orthopedic pins, clamps, screws and plates
   b. Clips (e.g., for use as hemostat)
   c. Staples
   d. Hooks, buttons and snaps
   e. Bone substitute (e.g., mandible prosthesis)
   f. Needles
   g. Non-permanant intrauterine devices (spermicide)
   h. Temporary draining or testing tubes or capillaries
   i. Surgical instruments
   j. Vascular implants or supports
   k. Vertebral discs
   l. Extracorporeal tubing for kidney and heart-lung machines
2. Fibrillar Products, knitted or woven, including velours
   a. Burn dressins
   b. Hernia patches
   c. Absorbent paper or swabs
   d. Medicated dressings
   e. Facial substitutes
   f. Gauze, fabric, sheet, felt or sponge for liver hemostasis
   g. Gauze bandages
   h. Dental packs
   i. Surgical sutures
3. Miscellaneous
   a. Flake or powder for burns or abrasions
   b. Foam as absorbable prosthesis
   c. Substitute for wire in fixations
   d. Film spray for prosthetic devices

B. Absorbable polymer in Combination with other Products

1. Solid Products, molded or machined
   a. Slowly digestible ion-exchange resin
   b. Slowly digestible drug release device (pill, pellet) as a repository, oral or implanted or intravaginal
   c. Reinforced bone pins, needles, etc.
2. Fibrillar Products
   a. Arterial graft or substituents
   b. Bandages for skin surfaces
   c. Burn dressings (in combination with other polymeric films)
   d. Coated sutures (i.e., a coating on a suture of this polymer)
   e. A coating of the present polymer on a suture of other material
   f. A two component suture, one being the present polymer, the components being spun or braided together
   g. Multicomponent fabrics or gauzes, the other component of which may be non-absorbable, or more rapidly absorbable.

The synthetic character and hence predicatable formability and consistency in characteristics obtainable from a controlled process are highly desirable.

One convenient method of sterilizing synthetic absorbable polymer prosthesis is by heat under such conditions that any microorganisms or deleterious materials are rendered inactive. Another common method is to sterilize using a gaseous sterilizing agent such as ethylene oxide. Other methods of sterilizing include radiation by X-rays, gamma rays, neutrons, electrons, etc., or high intensity ultrasonic vibrational energy or combinations of these methods. The present synthetic absorbable polymers may be sterilized by any of these methods, although there may be an appreciable but acceptable change in physical characteristics.

Other substances may be present, such as dyes, antibiotics, antiseptics, anaesthetics, and antioxidants. Surfaces can be coated with a silicone, beeswax, and the like to modify handling or absorption rate.

The absorbable polymer can be spun into fibers and used to form strands. Fibers of about 0.002 inch diameter are particularly convenient for fabrication. Sheets, or tubes from these absorbable polymer are wrapped around nerves, traumatically severed, to protect such nerves from invasive scar tissue growth, while the nerve is regenerating.

The ends or edges of mono-component or bi-component fabrics containing absorbable polymer may be rendered rigid by modling such edges, with or without additional solid absorbable polymer to a desired configuration. It is often easier to insert and retain flexible fabric prosthetic tube if the end of the tube is of a size and shape to be inserted into the severed end of a vessel.

In the case of extensive superficial abrasions, dressings, frequently gauze, pads or wrappings absorb blood or lymph and present a problem because the gauze dressings stick to the wound or are infiltrated by regenerated tissue. In the past, it has been customary to change dressings frequently to prevent such infiltration. Removing an adherent dressing can be quite painful.

Extensive surface abrasions such as from sliding on a concrete surface after falling off a motorcycle can be debrided and wrapped with a gauze synthetic absorbable polymer. The wound shows a tendency to bleed into the absorbable polymer gauze but the porosity of the gauze aids in rapidly stopping the flow of blood. By using several layers and permitting the blood to at least partially harden, a minimum amount of the absorbable polymer gauze is required and the main protective dressing is of ordinary cotton gauze wrapped around the injured area. A minimum of changing the dressing is required. The outer cotton gauze may be removed for inspection to be sure that infection does not occur, but the absorbable polymer gauze is allowed to remain in position, and partly heals into the tissue, and partly remains above the tissue. Fewer manipulative steps aid in preventing the entrance of new pathogens. After healing, the gauze below the new skin surface absorbs in the body and the non-absorbed gauze and the scab separate readily.

Poly(N-acetyl-D-glucosamine) is reported to be insoluble in all solvents except 88% phosphoric acid which badly degrades the polymer. Unexpectedly, it has now been found that hexafluoroisopropanol (HIPA) and hexafluoroacetone sesquihydrate (HFAS) are solvents for poly(N-acetyl-D-glucosamine). The solutions are quite viscous at 1.5% concentration and transparent. Clear, transparent films that are tough and very pliable when wet can be cast from these two fluorinated solvents. The films are easily removed from glass when wet. There is the appearance of crystalline regions as indicated by birefringence under a polarizing microscope. There was no indication of any polymer degradation in these solvents by infrared spectroscopic and nuclear magnetic resonance spectroscopic examination of the films.

The concentration of solution employed depends in part upon the desired thickness of a desired film. Thicknesses of anywhere from 0.5 mil to about 50 mils can be readily prepared. The films are tough, self-supporting films. The polyfluorinated solvents may be removed by evaporation in air, under reduced pressure, or by using a solvent, such as acetone, to wash out the polyfluorinated solvent. The casting surface is conveniently glass but may be stainless steel, poly(tetra-fluoroethylene), or other fluorinated polymer, on non-stick surface — even a liquid.

Elevated temperatures may be used. Poly(N-acetyl-D-glucosamine) decomposes on heating at about 220° C but may be heated to lower temperatures to speed the removal of the polyfluorinated solvent.

The solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisorpolyl alcohol and hexafluoroacetone sesquihydrate may be spun into filaments by standard techniques for wet or dry spinning. In a typical wet-spinning operation a solution or spinning dope of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate is extruded at a solution temperature from about room temperature up to about 60° C. through an appropriate orifice into a coagulated medium such as acetone or the solvents mentioned above. The coagulating liquid temperature may conveniently be at a temperature below that of the extrusion and may be very cold, well below 0° C. and may be any solvent or system in which the polymer coagulates and permits the ready removal of the solvent in the spinning dope.

It should be noted that although the boiling point of hexafluoroisopropyl alcohol is about 58° C. at atmospheric pressure, the boiling point of solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol will exceed 58° C. depending upon how much

polymer is dissolved in the solvent, and the pressure exerted on the system. Thus, solution temperatures and ranges of temperatures such as room temperature to 80° C. and similar ranges which appear throughout this specification contemplate the temperatures of solutions containing varying amounts of poly(N-acetyl-D-glucosamine) under pressures sufficient to elevate the boiling point of the solution into the upper limits of such temperature ranges.

Dilute solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate find utility as a vehicle for the measuring of viscosity and, hence, the determination of molecular weight and other physical characteristics of the polymer.

At the much thicker concentrations conveniently used for wet or dry spinning, the viscosity may become so high that extrusion is difficult amd the extrudability with available equipnent is a limiting factor on concentration.

The extrusion may be into the atmosphere, that is, dry spinning, with the hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate being removed by evaporation. The fibers may be wound as they harden; care being used to insure that the surface of the fiber is sufficiently hard that spinning dope does not adhere to equipment. The final treatment stages may be at higher temperatures with the limiting factor being decomposition of the polymer. Drying under vacuum speeds removal of the last traces of the polyfluorinated solvents.

Poly(N-acetyl-D-glucosamine) may be obtained in fibrillar form by precipitating a solution thereof in toluene. For instance, a 1.5% solution of poly(N-acetyl-D-glucosamine) in hexafluoroacetone sesquihydrate is precipitated by pouring it into toluene. After drying the material is similar in appearance and handling to dried cellulose pulp and is fibrillar in nature.

Fibers suitable for sutures and fabrics are manufactured by extruding a viscous solution of poly(N-acetyl-D-glucosamine) dissolved in hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate into a solvent bath. Solvents such as acetone, water, isopropanol, ether, other lower alcohols and other lower ketones are volatile, liquid at extrusion temperatures and low in cost.

The concentration of the poly(N-acetyl-D-glucosamine) in polyfluorinated solvent may be varied widely. Solutions as dilute as 0.01% may be used but to avoid the use of excess quantitites of the expensive polyfluorinated solvents, a concentration of about 0.5% to about 5% is usually preferred. Concentrations as high as 10% may be used, but at higher concentration, the solvent becomes quite viscous and it is often convenient to use a more dilute solution. Higher concentrations may be used if high pressure extruding equipment is available.

The extrusion is conveniently accomplished by wet extrusion into a solvent which aids in removing the hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate from the polymer. By washing with solvent, particularly at above room temperature, the hexafluoroacetone sesquihydrate and hexafluoroisopropyl alcohol are removed from the filaments or films formed. Because both hexafluoroisopropyl alcohol and hexafluoracetone sesquihydrate are known to be toxic, these should be washed out of polymers which are to be implanted in living tissue. Small quantities of the polyfluorinated solvents can be detected by gas chromatography or mass spectrometry so that an accurate evaluation of the effectiveness of washing may be made.

It is found that films and fibers of poly(N-acetyl-D-glucosamine) cast from hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate are not degraded by deionized water after 10 days exposure at ambient temperature. The same films immersed in a phosphate buffer containing 1500 units/ml of lysozyme at 37° C begin to degrade, although after 15 days, the films maintain their structure but are substantially degraded when observed by a microscope.

Both films and fibers of poly(N-acetyl-D-glucosamine) may be stretched, conveniently using heat, to orient the structure. Films and fibers of oriented structure are usually much stronger than unoriented films or fibers.

As the scope of this invention is broad, it is illustrated by the following typical examples in which temperatures are centigrade, and parts are by weight unless clearly otherwise specified.

EXAMPLE 1

Purification of Chitin

A commerical grade of chitin (Cal-Biochemicals) was finely ground in a ball mill overnight to pass a 6 mm screen and be retained by a 1 mm screen. 149 g. of this finely ground material was decalcified by extracting with 825 ml. of 2N HCl at 4° C for 48 hours, in a flask stirred with a magnetic stirrer. The material was collected by centrifugation and washed repeatedly with water until neutral. The ash content was 0.4–0.5%. The decalcified chitin was then stirred at room temperature with 1500 ml. of 90% formic acid overnight. The mixture was centrifuged and the residue repeatedly washed with water. The washed chitin was then suspended in 2 liters of 10% NaOH solution and heated at 90°–100° C. for 2.5 hours. The solution was filtered, the cake washed with water until neutral, washed several times with absolute ethanol and ether, and dried at 40° C. under reduced pressure; yield 66 g. of poly(N-acetyl-D-glucosamine). Infrared spectrum (KBr pellet) shows bands at 3500 cm^{-1} (S), 2900 (W), 1652 (S), 1619 (S), 1550 (S), 1370 (S), 1300 (M), 1070 (Broad). (S is strong, M is medium, W is weak).

EXAMPLE 2

Poly(N-Acetyl-D-Glucosamine) Matrix

Membranes of poly(N-acetyl-D-glucosamine) were prepared by dissolving poly(N-acetyl-D-glucosamine) from Example 1 in each of hexafluoroacetone sesquihydrate (1.4% solution) and hexafluoroisopropanol (2% solution), and casting on a glass plate. The last traces of solvent were evaporated off in a vacuum. The films were tough, transparent, non-tacky, flexible and were quite pliable when hydrated yet retained adequate strength to resist manipulation. The membranes showed no hydrolysis after exposure to water for 5 days. In the presence of lysozyme, however, the films were degraded slowly. The films as cast are suitable for use as absorbable barrier layers in surgery. They may be split and twisted to form sutures.

EXAMPLE 3

Dry Spinning Sutures

A spinning solution is prepared by dissolving three parts by weight of the poly(N-acetyl-D-glucosamine)

from Example 1 in 97 parts by weight of hexafluoroisopropyl alcohol. The solution is heated to about 55° C. with gentle stirring until the solution is accomplished. The thus formed solution is pumped through a spinnerette having 16 capillaries 100 microns in diameter and the spun fibers are passed through a nitrogen atmosphere until at last partially cool, and self-sustaining. The yarn formed is wound on a bobbin and stored hot under vacuum for several days. The yarn is then stretched to insure orientation and braided into a suture which is needled, wrapped on a reel, and stored in an open pack. The suture is sterilized by autoclaving at 30 lbs. steam for 15 minutes, and packaged in strippable envelopes.

EXAMPLE 4

Wet Spinning Sutures

A 3% solution of poly(N-acetyl-D-glucosamine) from Example 1 is prepared in hexfluoroacetone sesquihydrate by dissolving therein with heating and stirring. The resulting spinning dope is pumped through a 20 hole spinnerette having 100 microns capillary diameter into an acetone bath which is maintained below room temperature. The coagulated wet gel is pulled away from the spinning head and washed countercurrently with acetone. The coagulated gel is washed with additional acetone, then wound on a reel and subjected to vacujm at 50° C. until substantially all of the solvent is removed.

The yarn is hot stretched, then braided into a size 2/0 suture, needled, sterilized by autoclaving as in the preceding example, packaged and held for use.

Sutures from Examples 3 and 4, when used to sew up wounds in living tissue, are found to hold the tissues in place until healing sufficient to be self-supporting has accrued, and the sutures are later absorbed.

The surgical elements of poly(N-acetyl-D-glucosamine) can be sterilzied by conventional techniques such as autoclaving in the presence of live steam, or by dry heat, or ethylene oxide diluted with enough halofluoroalkane or carbon dioxide to be non-explosive, or by radiation by X-rays, gamma rays from cobalt, etc.

For human use, all surgical elements are to be sterile at time of use. For animal use, sterility should be maintained.

We claim:

1. A bone pin for the fixture of severed bone ends during regeneration after a traumatic or surgical fracture consisting essentially of a pin of poly(N-acetyl-D-glucosamine) of a diameter to fit into the medullary canal of a fractured bone end, either of natural size, or as drilled to a larger size, and a length of at least three times its diameter, whereby the bone pin is adapted to be a drive or friction fit in each bone end. so that the bone ends are held in fixed relationship in juxtaposition during regeneration of the bone, and the poly(N-acetyl-D-glucosamine) bone pin is later absorbed by the body fluids, permitting regeneration of marrow in the medullary canal.

2. A bone reinforcing plate of poly(N-acetyl-D-glucosamine) having high flexural strength and modulus, and a physical size of at least 1/16 inch by ¼ inch by 1 inch, and shaped to conform generally to the surface configuration of a bone, said plate having holes therein adapted to receive fasteners to hold the plate in adjacent reinforcing configuration to living bone, during a healing process, and later be absorbed by living tissue.

* * * * *

EXHIBIT 9

United States Patent [19]

Capozza

[11] **4,074,366**

[45] **Feb. 21, 1978**

[54] **POLY(N-ACETYL-D-GLUCOSAMINE) PRODUCTS**

[75] Inventor: **Richard Carl Capozza**, Norwalk, Conn.

[73] Assignee: **American Cyanamid Company**, Stamford, Conn.

[21] Appl. No.: **707,912**

[22] Filed: **July 22, 1976**

Related U.S. Application Data

[62] Division of Ser. No. 558,525, March 14, 1975, Pat. No. 3,989,535, which is a division of Ser. No. 441,717, Feb. 11, 1974, abandoned, which is a division of Ser. No. 558,526, March 14, 1975, Pat. No. 3,988,411.

[51] **Int. Cl.**[2] **A61F 1/00**

[52] **U.S. Cl.** **3/1**; 424/180

[58] **Field of Search** ..... 3/1; 128/92 C; 424/180

[56] **References Cited**

U.S. PATENT DOCUMENTS

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Primary Examiner—Leland A. Sebastian
Attorney, Agent, or Firm—Charles F. Costello, Jr.

[57] **ABSTRACT**

Poly(N-acetyl-D-glucosamine) is soluble in hexafluoroisopropyl alcohol and hexafluoracetone sesquihydrate. The solutions formed may be wet or dry spun into filaments, or cast into films or solid articles, which may be used as absorbable surgical sutures, or other absorbable surgical elements. Poly(N-acetyl-D-glucosamine) is enzymatically degradable in living tissue, and is resistant to hydrolytic degradation, and, therefore, surgical elements thereof have good storage characteristics under a wide variety of conditions.

3 Claims, No Drawings

POLY(N-ACETYL-D-GLUCOSAMINE) PRODUCTS

This is a division, of application Ser. No. 558,525, filed Mar. 14, 1975, U.S. Pat. No. 3,989,535, which is a division of application Ser. No. 441,717, filed Feb. 11, 1974 now abandoned. Another divisional of said Ser. No. 441,717 is application Ser. No. 558,526, filed Mar. 14, 1975, U.S. Pat. No. 3,988,411.

BACKGROUND OF THE INVENTION

Poly(N-acetyl-D-glucosamine) is a known polymer which is a component of naturally occurring chitin. It is regarded as insoluble in conventional solvents, and, therefore, has been used as a powder. There is a demand for absorbable surgical elements, particularly sutures, which are strong enough to serve as a tissue retaining element during a healing process, and which then are absorbed by the living tissue. Requirements for the duration of useful strength vary widely with both the type of tissue and the surgical procedure. Some cosmetic purposes require strength for only a few hours or a few days. Other uses require strength for periods of months or even years. Advantageously, the surgical element should absorb promptly after it has served its useful function. Sutures have long been treated with dyes and therapeutic agents, poly(N-acetyl-D-glucosamine) sutures may be so treated.

Absorbable surgical elements usually start losing strength almost as soon as implanted, but a useful degree of strength is maintained for a much longer period. Complete absorption is, of course, much slower. Sharp changes in strength with time are not to be expected.

DESCRIPTION OF THE PRIOR ART

U.S. Pat. No. 3,297,033, Schmitt and Polistina, Jan. 10, 1967, SURGICAL SUTURES, discloses polyhydroxyacetic ester absorbable sutures. The material is also called polyglycolic acid, and is disclosed as permitting small quantities of comonomers to be present, such as dl-lactic acid, its optically active forms, homologs and analogs. A small quantity is recognized by the art as up to 15%, as shown by U.S. Pat. No. 2,668,162, Lowe, Feb. 2, 1954, PREPARATION OF HIGH MOLECULAR WEIGHT POLYHYDROXY-ACETIC ESTER.

Many uses of polyglycolic acid for surgical purposes are disclosed in said U.S. Pat. No. 3,297,033 and continuations-in-part thereof including: U.S. Pat. No. 3,463,158, Schmitt and Polistina, Aug. 26, 1969, POLYGLYCOLIC ACID PROSTHETIC DEVICES; U.S. Pat. No. 3,620,218, Schmitt and Polistina, Nov. 16, 1971, CYLINDRICAL PROSTHETIC DEVICES OF POLYGLYCOLIC ACID; U.S. Pat. No. 3,739,773, Schmitt and Polistina, June 19, 1973, POLYGLYCOLIC PROSTHETIC DEVICES; and U.S. Ser. No. 365,656, Schmitt and Polistina, May 31, 1973, SURGICAL DRESSINGS OF ABSORBABLE POLYMERS.

U.S. Pat. No. 3,463,158, Schmitt and Polistina, Aug. 26, 1969, POLYGLYCOLIC ACID PROSTHETIC DEVICES, discloses surgical uses of polyglycolic acid, and incorporates definitions of some terms.

U.S. Pat. No. 3,620,218, Schmitt and Polistina, November 16, 1971, CYLINDRICAL PROSTHETIC DEVICES OF POLYGLYCOLIC ACID, lists many surgical uses of polyglycolic acid.

U.S. Pat. No. 3,737,440, Schmitt and Bailey, June 5, 1973, POLYGLYCOLIC ACIDS IN SOLUTIONS, discloses hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate as solvents for the preparation of solutions of polyglycolic acid, and wet and dry casting of such solutions. Polyglycolic acid has many surgical uses as an absorbable polymer.

Polyglycolic acid sutures are the only synthetic absorbable sutures that have met with commercial surgical acceptance to date.

Chitin has been estimated to be the second most abundant polysaccharide in nature with a synthesis in the neighborhood of a billion tons a year by marine organisms. See Chitin, N. V. Tracey, Reviews of Pure and Applied Chemistry, Royal Australian Chemical Institute, Vol. 7, No. 1, March, 1957, pages 1 to 14.

Carboxymethylchitin is disclosed in Carbohyd, Res. 7, 483–485 (1968), Ralph Trujillo.

This article mentions the hydrolysis of both chitin and carboxymethylchitin by lysozyme.

I. Joffe and H. R. Hepburn, "Observations on Regenerated Chitin Films," J. Materials Science, 8 (1973), 1751–1754, give values on the strength of films of regenerated chitin, from a chitin xanthate dispersion — including a comparison of strength after 30 years storage. Values as high as $9.31 \times 10^7 Nm^{-2}$ are given (calculates to 6.3×10^3 pounds/sq. inch).

Noguchi, Wada, Seo, Tokura and Nishi, "Studies on Chitin and Chitin-Cellulose Fibers," Kobunshi Kagaku, Vol. 30, No. 338, pp. 320–326 and 378, (June 1973) disclose chitin fibers spun by a xanthate process, analogous to the spinning of cellulose to form rayon. A 50% chitin-cellulose fiber is disclosed with a denier of 12.3 and a tenacity of 1.08 grams/denier dry and 0.13 grams/denier wet.

Poly(N-acetyl-D-glucosamine) differs from cellulose in that instead of a hydroxyl group in the 2 position on cellulose, there is an acetylamino group.

Prudden, Migel, Hanson, Freidrich and Balassa in "The Discovery of a Potent Pure Chemical Wound-Healing Accelerator," The American Journal of Surgery, Vol. 119, May 1970, pages 560 to 564, disclose that chitin containing n-acetyl glucosamine is useful to accelerate wound-healing. These authors postulate fibers of a long chain n-acetyl glucosamine as a nonabsorbable suture, and a shorter polymer length as an absorbable suture. Other prosthetic devices, such as hemostatic clips, vascular and joint protheses, mesh and knit abdominal thoracic wall replacements are postulated for evaluation. No methods are postulated for the achievements of these objectives.

The above patents and articles are herein hereby incorporated by this reference thereto for background information on chitin, its properties and derivatives.

SUMMARY OF THE INVENTION

This invention relates to solid surgical elements of poly(N-acetyl-D-glucosamine), methods of making them, and more particularly to polymers which are compatible with living mammalian tissue, particularly human tissue, and which can be used surgically, and are biologically degradable into tissue compatible components which are absorbed by living tissues. The primary degradation of the polymer is by enzymatic fission into products which can be carried away by the living tissue and which products are degradable to excretable components or are themselves excretable. Because of the surgical demand for sutures, absorbable fabrics, gauzes,

bone pins, etc. whose absorption and strength characteristics vary, it is desirable that a spectrum of strength and absorbability characteristics be provided to meet surgical demands for various procedures. The enzyme lysozyme is particularly effective in the enzymatic degradation of poly(N-acetyl-D-glucosamine). Various forms of poly(N-acetyl-D-glucosamine) may have different degradation rates, and the degradation rate may vary with the location.

Poly(N-acetyl-D-glucosamine) has many advantages as a material of construction for sutures and other surgical elements. The poly(N-acetyl-D-glucosamine) in its own right tends to encourage wound healing rather than slow it down. Poly(N-acetyl-D-glucosamine) is biodegradable by enzymatic action with minimal tissue reaction.

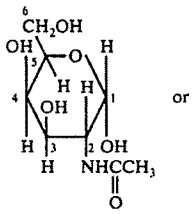
Surgical elements of poly(N-acetyl-D-glucosamine) are not hydrolyzed by water and, hence, need not be kept bone dry but may be stored under ambient conditions of moisture for prolonging periods of time. The basic poly(N-acetyl-D-glucosamine) may be modified by treatment to introduce carboxymethyl, hydroxyethyl or O-ethyl substituents so that the polymer has linkages from acetyl-6-O-(carboxymethyl)-D-glucosamine units, acetyl-6-O-(2'-hydroxyethyl)-D-glucosamine units, or acetyl-6-O-(ethyl)-D-glucosamine units. Since modification by the introduction of these derivatives alters the rate of enzymatic degradation, such introduction provides a means for controlling the absorption rate as well as making the surgical element more hydrophilic or more hydrophobic to an extent desire.

Other side chains may be placed on the glucosamine ring, or its substituents because the side chains may vary from methyl to long chain alkyl, including branched chains, unsaturated chains, aryl or aralkyl, and which may include halogen, alkoxy, aryloxy, aralkoxy, ether, ester and amide groups, as substituents on the side chains, the relative distribution between aqueous and solvent components in a system can be varied as well as water solubility or oil and solvent solubility. Also, because the size and location of the side chains affects the rate of degradation and the acidity of the system, the rate of enzymatic degradation can be varied over wide limits to meet the requirements of a system and the desires of the operator. The less highly substituted materials are often preferred for medical uses. The broader range of substituents permits more flexibility in pH control, and in biodegradable polymers for use in packaging, etc. The use of side chains with unsaturated linkages permits crosslinked polymers to be formed. This uniformity results in greater strength, more crystallinity, and more readily reproducible and controllable characteristics, which are of interest to a surgeon during use.

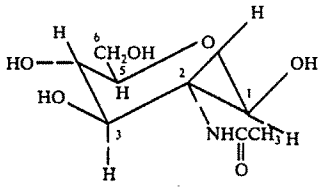
Fibers made by extruding solutions of poly(N-acetyl-D-glucosamine) in polyfluorinated solvents such as hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate or mixtures of such solvents permit dry or wet spinning of fibers which are of a convenient size for forming sutures.

The fibers are more pliable when wet with water. The enhanced pliability, when wet with water, is highly advantageous in that many surgeons are accustomed to handling catgut which must be wet with water to have adequate handleability and, hence, are using familiar techniques and procedures in surgery. Monofilaments are usable when wet. A dry braided construction of polyfilamentary character is frequently advantageous.

Poly(N-acetyl-D-glucosamine) has the formula:

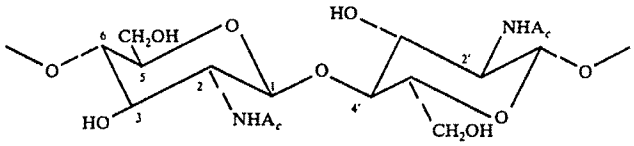


or



Groups below the plane of the paper are shown by a dotted bond.

Poly(N-acetyl-D-glucosamine) has ascribed to it the formula (ring hydrogens omitted for clarity):



Poly(N-acetyl-D-glucosamine) is a major component of naturally occurring chitin. The naturally occurring material has not only the poly(N-acetyl-D-glucosamine) but also inorganic salts thought to be forms of calcium carbonate and proteinaceous material, the composition of which is not presently known. The term "chitin" is used herein to refer to the various naturally occurring forms of chitin including the protein and inorganic carbonate components. The term "purified chitin" is used to refer to chitin after purification to remove calcium carbonate and other inorganic salts and various proteins which may be present and is essentially poly(N-acetyl-D-glucosamine). Some confusion exists in the literature in that the name chitin is used as a name for poly(N-acetyl-D-glucosamine) without specifying whether it is a naturally occurring material containing inorganic salts and proteins or whether the term is intended to designate purified poly(N-acetyl-D-glucosamine) without specifying the degree of purity or the character of the impurities present.

The term "drug" is used to refer to a substance other than a food intended to affect the structure or function of the body of man or other animal. The term is somewhat broader than "medicine" in that the term "medicine" is sometimes considered to be restricted to an

agent which is administered to affect or control a pathogenic condition.

The term "enzymatically degradable" refers to a form of poly(N-acetyl-D-glucosamine) or its derivatives which is broken down into body fluid soluble components. The problem of retention by the body or disposal of the residual matrix is minimal or non-existent.

While other enzymes may also affect the enzymatic degradation of the poly(N-acetyl-D-glucosamine) matrix, the enzyme which is most widely distributed in the body and here very effective is lysozyme. Lysozyme occurs in practically all of the body fluids and effectively breaks down the polymer chain to water soluble or disposable components.

Poly(N-acetyl-D-glucosamine) is not readily hydrolyzed by water.

It is highly advantageous to have the degradation of the poly(N-acetyl-D-glucosamine) occur only by the action of an enzyme as the resistance to hydrolytic degradation markedly reduces problems of manufacture and storage in the presence of ambient moisture, and ensures a steady smooth surface erosion rather than a fragmentation process commonly experienced by polymers which are hydrolyzed by small molecules.

The degradation rate of poly(N-acetyl-D-glucosamine) can be lowered by crosslinking, if a slower rate is preferred.

In general, the surgical uses of the polymers of the present invention are similar to those previously taught for polyglycolic acid and as set forth in U.S. Pat. Nos. 3,297,033; 3,463,158; 3,620,218; and 3,739,773, and U.S. Ser. No. 365,656, supra. These disclosures of uses are herein hereby incorporated by this reference thereto.

These uses are extremely varied. For clarity and explanation, certain terms are defined and representative uses given for the novel polymer forms.

A "filament" is a single, long, thin flexible structure of a non-absorbable or absorbable material. It may be continuous or staple.

"Staple" is used to designate a group of shorter filaments which are usually twisted together to form a longer continuous thread.

An absorbable filament is one which is absorbed, that is, digested or dissolved, in living mammalian tissue.

A "thread" is a plurality of filaments, either continuous or staple, twisted together.

A "strand" is a plurality of filaments or threads twisted, plaited, braided, or laid parallel to form a unit for further construction into a fabric, or used per se, or a monofilament of such size as to be woven or used independently.

A "fabric" is a three dimensional assembly of filaments, which may be woven, knitted, felted or otherwise formed into a flexible sheet having two layer dimensions and a thinner thickness dimension. A fabric may be cut to a desired size before or at the time of use.

Except where limited specifically or by context, the word fabric includes both absorbable and non-absorbable cloth, or a fabric or cloth that is partially of absorbable polymer.

A "dressing" is a woven, knitted, felted or braided fabric, of at least one layer, which is designed to protect a wound and favor its healing. As used herein, the term dressing includes bandages, insofar as they contact the wound itself. The dressing may be entirely internal.

A "bandage" is a strip of gauze, or other material used to hold a dressing in place, to apply pressure, to immobilize a part, to obliterate tissue cavities or to check hemorrhage. Except insofar as the bandage comes in contact with a wound, or the exudate from a wound, there is no need for the bandage to be of absorbable polymer. If the bandage may be in a position where absorbability by living tissue of at least part of the bandage is desirable, at least that part should be of absorbable polymer.

The dressing may be in part directive of growth, as, for example, in nerve tissue, which grows slowly, and as a result has regeneration impaired by the more rapid growth of scar tissue which can block the growth of the nerve tissue. With a wrap-around sheath of absorbable polymer fabric or a split or solid tube used to support, place, hold and protect; regeneration of nerve tissue and function is greatly aided. Other factors may inhibit regeneration of nerve tissue or function, but with the exclusion of scar tissue, such other factors may be separately treated.

For different purposes and in different types of tissue the rate of absorption may vary. In general, an absorbable suture or solid load bearing prosthesis should have as high a portion of its original strength as possible for at least 3 days, and sometimes as much as 30 days or more, and preferably should be completely absorbed by muscular tissue within from 45 to 90 days or more depending on the mass of the cross-section. The rate of absorption in other tissues may vary even more.

For dressings, strength is often a minimal requirement. Some dressings, as for instance, on a skin abrasion, may need strength for only a few hours, until a scab forms, and rapid decrease of strength and absorption is an advantage so that when the scab is ready to fall off, the dressing does not cause a delay. For burns, and larger lesions, strength and reinforcement may be desired for a longer period.

In common with many biological systems, the requirements are not absolute and the rate of absorption as well as the short-term strength requirement varies from patient to patient and at different locations within the body, as well as with the thickness of the section of the polymer.

The absorbable polymer may be formed as tubes or sheets for surgical repair and may also be spun as thin filaments and woven or felted to form absorbable sponges or absorbable gauze, or used in conjunction with other compressive structures as prosthetic devices within the body of a human or animal where it is desirable that the structure have short-term strength, but be absorbable. The useful embodiments include tubes, including branched tubes or Tees, for artery, vein or intestinal repair, nerve splicing, tendon splicing, sheets for tying up and supporting damaged kidney, liver and other intestinal organs, protecting damaged surface areas such as abrasions, particularly major abrasions, or areas where the skin and underlying tissues are damaged or surgically removed.

In surgical techniques involving internal organs, hemorrhage may be a major problem. Some of the organs have such tissue characteristics that it is very difficult to use sutures or ligatures to prevent bleeding. For example, the human liver may suffer traumatic damage or exhibit tumors or for other reasons require surgery. In the past it has been very difficult to excise part of the liver or to suture the liver without the combined problems of the sutures cutting out and hemorrhage at the surface causing such major complications as to either prevent surgery or cause an unfavorable prognosis.

It is now found that a sponge or pad or velour of the present absorbable polymer may be used to protect the surface and permit new feats of surgical intervention. For instance, filaments may be formed into a woven gauze or felted sponge or a velour, preferably the construction is fairly tight by textile standards, and such sponge may be placed on the surface of the bleeding organ such as the liver or a lung with either gentle suturing or with ties in the nature of ligatures to hold the element in position with a certain amount of body fluids flowing into the sponge and being absorbed, which results in hemostasis and prevention of further loss of body fluids. If a liver or lung is so repaired, the organ may be replaced in the body cavity and the wound closed.

Where surgically useful, the sponge or fabric can be used as a bolster to prevent a suture from cutting out. For instance, if the liver is to be sutured, an absorbable polymer pad can be placed on the surfaces to reinforce the tissue and prevent the suture from cutting into rather than retaining the tissue. Such pads of gauze or felt protect tissue from cutting.

Absorbable pads, bandages or sponges are extremely useful in surgical techniques in which it is the intent to remove the major portion or all of such sponges, felt or pads but, through inadvertence or accident, part of it may remain. For instance, in a surgical operation one of the problems which arises is the lint from cotton sponges remaining in the wound. If absorbable polymer sponges are used, any small fragments which are accidentally displaced are absorbed without incident and even if a sponge is left in the wound, the deleterious effects are minimal.

The use of a synthetic absorbable polymer as a sponge or pad is particularly advantageous for surface abrasions. In the past it has been necessary to put on a dressing and avoid having the non-absorbable dressing grow into the tissue at all costs. If elements of an absorbable polymer gauze are beneath the regenerating tissue level, the tissue will regenerate and absorb the polymer with the residual polymer in the scab falling off when the scab is displaced.

The dressing that contacts tissue should be sterile. A strippable sterile package is a convenient storage system to maintain sterility between the time of manufacture and time of use.

Even in cosmetic surgery or skin surgery, where in the past it has been quite customary to use silk sutures and, after the tissue in regenerated sufficient to be self-retaining, remove the sutures so that they do not leave scars, the use of synthetic absorbable polymer sutures now permits implantation of sutures through the skin with the part below the skin surface being absorbed and the part above the skin surface falling off. The resulting minimal degree of scarring at the skin surface is highly advantageous.

In surgery various tissues need to be retained in position during healing. Defects and wounds of the abdominal wall, chest wall and other such tissues need to be reconstructed. For a hernia, a permanent splice or reinforcement is often desired as shown in Usher, U.S. Pat. No. 3,054,406, SURGICAL MESH, or U.S. Pat. No. 3,124,136, METHOD OF REPAIRING BODY TISSUE. For some surgical procedures, a temporary reinforcing is desired to provide strength while body tissues are healing; and after the body tissues have assumed the load, foreign components are no longer desired. Tissue retention using the general techniques disclosed in the Usher patents, supra, are readily accomplished using either an absorbable synthetic polymer monofilament or polyfilament fabric or mesh or by using a non-absorbable material such as polyethylene or polypropylene or polyester woven as a bicomponent mesh or kit with an absorbable synthetic polymer. The use of a bicomponent fabric has the advantage of giving additional early strength for holding the tissues in position during initial regeneration with the absorbable portions being absorbed, thus permitting body tissues to invade and reinforce the permanent mesh.

In common with other surgical procedures, it is often desirable that a bicomponent structure be used which provides the spacing desired for non-absorbable elements, with the absorbable synthetic polymer element holding the structure in a desired geometrical configuration at the start of the healing process. As the element is absorbed, regenerating tissue invades and replaces the dissolved synthetic polymer so that the non-absorbed element is left in a desired configuration, interlaced with living tissue in a stress-transferring relationship.

The choice of a non-absorbable reinforcement, a partially absorbable reinforcement, or a completely absorbable reinforcement is a matter of surgical judgment, based upon the condition of the patient, the body structure under treatment, and other medical factors.

For instance, a synthetic absorbable polymer sponge may be used in a cavity after tooth extraction to stanch the flow of blood. The sponge is either absorbed by regenerating tissue, or disintegrates into the mouth, permitting improved recovery after extractions.

The medical uses of the polymers of the present invention include, but are not necessarily limited to:

A. Absorbable polymer alone

1. Solid Products, molded or machined
   a. Orthopedic pins, clamps, screws and plates
   b. Clips (e.g., for use as hemostat)
   c. Staples
   d. Hooks, buttons and snaps
   e. Bone substitute (e.g., mandible prosthesis)
   f. Needles
   g. Non-permanent intrauterine devices (spermicide)
   h. Temporary draining or testing tubes or capillaries
   i. Surgical instruments
   j. Vascular implants or supports
   k. Vertebral discs
   l. Extracorporeal tubing for kidney and heart-lung machines.

2. Fibrillar Products, knitted or woven, including velours
   a. Burn dressings
   b. Hernia patches
   c. Absorbent paper or swabs
   d. Medicated dressings
   e. Facial substitutes
   f. Gauze, fabric, sheet, felt or sponge for liver hemostasis
   g. Gauze bandages
   h. Dental packs
   i. Surgical sutures

3. Miscellaneous
   a. Flake or powder for burns or abrasions
   b. Foam as absorbable prosthesis
   c. Substitute for wire in fixations
   d. Film spray for prosthetic devices

B. Absorbable polymer in Combination with other Products

1. Solid Products, molded or machined
a. Slowly digestible ion-exchange resin
b. Slowly digestible drug release device (pill, pellet) as a repository, oral or implanted or intravaginal
c. Reinforced bone pins, needles, etc.
2. Fibrillar Products
a. Arterial graft or substituents
b. Bandages for skin surfaces
c. Burn dressings (in combination with other polymeric films)
d. Coated sutures (i.e., a coating on a suture of this polymer)
e. A coating of the present polymer on a suture of other material
f. A two component suture, one being the present polymer, the components being spun or braided together
g. Multicomponent fabrics or gauzes, the other component of which may be non-absorbable, or more rapidly absorbable.

The synthetic character and hence predictable formability and consistency in characteristics obtainable from a controlled process are highly desirable.

One convenient method of sterilizing synthetic absorbable polymer prosthesis is by heat under such conditions that any microorganisms or deleterious materials are rendered inactive. Another common method is to sterilize using a gaseous sterilizing agent such as ethylene oxide. Other methods of sterilizing include radiation by X-rays, gamma rays, neutrons, electrons, etc., or high intensity ultrasonic vibrational energy or combinations of these methods. The present synthetic absorbable polymers may be sterilized by any of these methods, although there may be an appreciable but acceptable change in physical characteristics.

Other substances may be present, such as dyes, antibiotics, antiseptics, anaesthetics, and antioxidants. Surfaces can be coated with a silicone, beeswax, and the like to modify handling or absorption rate.

The absorbable polymer can be spun into fibers and used to form strands. Fibers of about 0.002 inch diameter are particularly convenient for fabrication. Sheets, or tubes from these absorbable polymer are wrapped around nerves, traumatically severed, to protect such nerves from invasive scar tissue growth, while the nerve is regenerating.

The ends or edges of mono-component or bi-component fabrics containing absorbable polymer may be rendered rigid by molding such edges, with or without additional solid absorbable polymer to a desired configuration. It is often easier to insert and retain a flexible fabric prosthetic tube if the end of the tube is of a size and shape to be inserted into the severed end of a vessel.

In the case of extensive superficial abrasions, dressings, frequently gauze, pads or wrappings absorb blood or lymph and present a problem because the gauze dressings stick to the wound or are infiltrated by regenerated tissue. In the past, it has been customary to change dressings frequently to prevent such infiltration. Removing an adherent dressing can be quite painful.

Extensive surface abrasions such as from sliding on a concrete surface after falling off a motorcycle can be debrided and wrapped with a gauze synthetic absorbable polymer. The wound shows a tendency to bleed into the absorbable polymer gauze but the porosity of the gauze aids in rapidly stopping the flow of blood. By using several layers and permitting the blood to at least partially harden, a minimum amount of the absorbable polymer gauze is required and the main protective dressing is of ordinary cotton gauze wrapped around the injured area. A minimum of changing the dressing is required. The outer cotton gauze may be removed for inspection to be sure that infection does not occur, but the absorbable polymer gauze is allowed to remain in position, and partly heals into the tissue, and partly remains above the tissue. Fewer manipulative steps aid in preventing the entrance of new pathogens. After healing, the gauze below the new skin surface absorbs in the body and the non-absorbed gauze and the scab separate readily.

Poly(N-acetyl-D-glucosamine) is reported to be insoluble in all solvents except 88% phosphoric acid which badly degrades the polymer. Unexpectedly, it has now been found that hexafluoroisopropanol (HIPA) and hexafluoroacetone sesquihydrate (HFAS) are solvents for poly(N-acetyl-D-glucosamine). The solutions are quite viscous at 1.5% concentration and transparent. Clear, transparent films that are tough and very pliable when wet can be cast from these two fluorinated solvents. The films are easily removed from glass when wet. There is the appearance of crystalline regions as indicated by birefringence under a polarizing microscope. There was no indication of any polymer degradation in these solvents by infrared spectroscopic and nuclear magnetic resonance spectroscopic examination of the films.

The concentration of solution employed depends in part upon the desired thickness of a desired film. Thicknesses of anywhere from 0.5 mil to about 50 mils can be readily prepared. The films are tough, self-supporting films. The polyfluorinated solvents may be removed by evaporation in air, under reduced pressure, or by using a solvent, such as acetone, to wash out the polyfluorinated solvent. The casting surface is conveniently glass but may be stainless steel, poly(tetra-fluoroethylene), or other fluorinated polymer, or non-stick surface — even a liquid.

Elevated temperatures may be used. Poly(N-acetyl-D-glucosamine) decomposes on heating at about 220° C but may be heated to lower temperatures to speed the removal of the polyfluorinated solvent.

The solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate may be spun into filaments by standard techniques for wet or dry spinning. In a typical wet-spinning operation a solution or spinning dope of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate is extruded at a solution temperature from about room temperature up to about 60° C. through an appropriate orifice into a coagulated medium such as acetone or the solvents mentioned above. The coagulating liquid temperature may conveniently be at a temperature below that of the extrusion and may be very cold, well below 0° C. and may be any solvent or system in which the polymer coagulates and permits the ready removal of the solvent in the spinning dope.

It should be noted that although the boiling point of hexafluoroisopropyl alcohol is about 58° C. at atmospheric pressure, the boiling point of solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol will exceed 58° C. depending upon how much polymer is dissolved in the solvent, and the pressure

exerted on the system. Thus, solution temperatures and ranges of temperatures such as room temperature to 80° C. and similar ranges which appear throughout this specification contemplate the temperatures of solutions containing varying amounts of poly(N-acetyl-D-glucosamine) under pressures sufficient to elevate the boiling point of the solution into the upper limits of such temperature ranges.

Dilute solutions of poly(N-acetyl-D-glucosamine) in hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate find utility as a vehicle for the measuring of viscosity and, hence, the determination of molecular weight and other physical characteristics of the polymer.

At the much thicker concentrations conveniently used for wet or dry spinning, the viscosity may become so high that extrusion is difficult and the extrudability with available equipment is a limiting factor on concentration.

The extrusion may be into the atmosphere, that is, dry spinning, with the hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate being removed by evaporation. The fibers may be wound as they harden; care being used to insure that the surface of the fiber is sufficiently hard that spinning dope does not adhere to equipment. The final treatment stages may be at higher temperatures with the limiting factor being decomposition of the polymer. Drying under vacuum speeds removal of the last traces of the polyfluorinated solvents.

Poly(N-acetyl-D-glucosamine) may be obtained in fibrillar form by precipitating a solution thereof in toluene. For instance, a 1.5% solution of poly(N-acetyl-D-glucosamine) in hexafluoroacetone sesquihydrate is precipitated by pouring it into toluene. After drying, the material is similar in appearance and handling to dried cellulose pulp and is fibrilar in nature.

Fibers suitable for sutures and fabrics are manufactured by extruding a viscous solution of poly(N-acetyl-D-glucosamine) dissolved in hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate into a solvent bath. Solvents such as acetone, water, isopropanol, ether, other lower alcohols and other lower ketones are volatile, liquid at extrusion temperatures and low in cost.

The concentration of the poly(N-acetyl-D-glucosamine) in polyfluorinated solvent may be varied widely. Solutions as dilute as 0.01% may be used but to avoid the use of excess quantities of the expensive polyfluorinated solvents, a concentration of about 0.5% to about 5% is usually preferred. Concentrations as high as 10% may be used, but at higher concentration, the solvent becomes quite viscous and it is often convenient to use a more dilute solution. Higher concentrations may be used if high pressure extruding equipment is available.

The extrusion is conveniently accomplished by wet extrusion into a solvent which aids in removing the hexafluoroisopropyl alcohol and hexafluoroacetone sesquihydrate from the polymer. By washing with solvent, particularly at above room temperature, the hexafluoroacetone sesquihydrate and hexafluoroisopropyl alcohol are removed from the filaments or films formed. Because both hexafluoroisopropyl alcohol and hexafluoracetone sesquihydrate are known to be toxic, these should be washed out of polymers which are to be implanted in living tissue. Small quantities of the polyfluorinated solvents can be detected by gas chromatography or mass spectrometry so that an accurate evaluation of the effectiveness of washing may be made.

It is found that films and fibers of poly(N-acetyl-D-glucosamine) cast from hexafluoroisopropyl alcohol or hexafluoroacetone sesquihydrate are not degraded by deionized water after 10 days exposure at ambient temperature. The same films immersed in a phosphate buffer containing 1500 units/ml of lysozyme at 37° C begin to degrade, although after 15 days, the films maintain their structure but are substantially degraded when observed by a microscope.

Both films and fibers of poly(N-acetyl-D-glucosamine) may be stretched, conveniently using heat, to orient the structure. Films and fibers of oriented structure are usually much stronger than unoriented films or fibers.

As the scope of this invention is broad, it is illustrated by the following typical examples in which temperatures are centigrade, and parts are by weight unless clearly otherwise specified.

EXAMPLE 1

Purification of Chitin

A commercial grade of chitin (Cal-Biochemicals) was finely ground in a ball mill overnight to pass a 6 mm screen and be retained by a 1 mm screen. 149 g. of this finely ground material was decalcified by extracting with 825 ml. of 2N HCl at 4° C for 48 hours, in a flask stirred with a magnetic stirrer. The material was collected by centrifugation and washed repeatedly with water until neutral. The ash content was 0.4–0.5%. The decalcified chitin was then stirred at room temperature with 1500 ml. of 90% formic acid overnight. The mixture was centrifuged and the residue repeatedly washed with water. The washed chitin was then suspended in 2 liters of 10% NaOH solution and heated at 90°–100° C. for 2.5 hours. The solution was filtered, the cake washed with water until neutral, washed several times with absolute ethanol and ether, and dried at 40° C. under reduced pressure; yield 66 g. of poly(N-acetyl-D-glucosamine). Infrared spectrum (KBr pellet) shows bands at 3500 cm^{-1} (S), 2900 (W), 1652 (S), 1619 (S), 1550 (S), 1370 (S), 1300 (M), 1070 (Broad). (S is strong, M is medium, W is weak).

EXAMPLE 2

Poly(N-Acetyl-D-Glucosamine) Matrix

Membranes of poly(N-acetyl-D-glucosamine) were prepared by dissolving poly(N-acetyl-D-glucosamine) from Example 1 in each of hexafluoroacetone sesquihydrate (1.4% solution) and hexafluoroisopropanol (2% solution), and casting on a glass plate. The last traces of solvent were evaporated off in a vacuum. The films were tough, transparent, non-tacky, flexible and were quite pliable when hydrated yet retained adequate strength to resist manipulation. The membranes showed no hydrolysis after exposure to water for 5 days. In the presence of lysozyme, however, the films were degraded slowly. The films as cast are suitable for use as absorbable barrier layers in surgery. They may be split and twisted to form sutures.

EXAMPLE 3

Dry Spinning Sutures

A spinning solution is prepared by dissolving three parts by weight of the poly(N-acetyl-D-glucosamine) from Example 1 in 97 parts by weight of hexafluoroisopropyl alcohol. The solution is heated to about 55° C.

with gentle stirring until the solution is accomplished. The thus formed solution is pumped through a spinnerette having 16 capillaries 100 microns in diameter and the spun fibers are passed through a nitrogen atmosphere until at least partially cool, and self-sustaining. The yarn formed is wound on a bobbin and stored hot under vacuum for several days. The yarn is then stretched to insure orientation and braided into a suture which is needled, wrapped on a reel, and stored in an open pack. The suture is sterilized by autoclaving at 30 lbs. steam for 15 minutes, and packaged in strippable envelopes.

EXAMPLE 4

Wet Spinning Sutures

A 3% solution of poly(N-acetyl-D-glucosamine) from Example 1 is prepared in hexafluoroacetone sesquihydrate by dissolving therein with heating and stirring. The resulting spinning dope is pumped through a 20 hole spinnerette having 100 microns capillary diameter into an acetone bath which is maintained below room temperature. The coagulated wet gel is pulled away from the spinning head and washed countercurrently with acetone. The coagulated gel is washed with additional acetone, then wound on a reel and subjected to vacuum at 50° C. until substantially all of the solvent is removed.

The yarn is hot stretched, then braided into a size 2/0 suture, needled, sterilized by autoclaving as in the preceding example, packaged and held for use.

Sutures from Examples 3 and 4, when used to sew up wounds in living tissue, are found to hold the tissues in place until healing sufficient to be self-supporting has accrued, and the sutures are later absorbed.

The surgical elements of poly(N-acetyl-D-glucosamine) can be sterilized by conventional techniques such as autoclaving in the presence of live steam, or by dry heat, or ethylene oxide diluted with enough halofluoroalkane or carbon dioxide to be non-explosive, or by radiation by X-rays, gamma rays from cobalt, etc.

For human use, all surgical elements are to be sterile at time of use. For animal use, sterility should be maintained.

We claim:

1. A surgical prosthesis comprising non-absorbable filaments shaped as a living tissue reinforcing element, and mixed with and coacting with said non-absorbable filaments, in at least a part of the element, a structure consisting essentially of poly(N-acetyl-D-glucosamine), whereby on implantation in living tissue, the poly(N-acetyl-D-glucosamine) is absorbed by the living tissue which replaces the poly(N-acetyl-D-glucosamine) and interlocks with the non-absorbable filaments, said prosthesis being sterile at time of implantation.

2. The prosthesis of claim 1 in which the reinforcing element comprises a non-absorbable strand fabric mesh section, and interwoven and graded thereinto, bicomponent strands in a graded transition portion, the individual strands of which are of proportionately increasing poly(N-acetyl-D-glucosamine) and decreasing non-absorbable filament composition, at increasing distances from said non-absorbable strand fabric mesh section.

3. An absorbable prosthesis for the anastomosis of vessels in the tissue of a living mammal consisting essentially of a hollow cylinder of poly(N-acetyl-D-glucosamine), having an inner diameter approximately the same as the inner diameter of the subject vessel, and a smooth outer surface of a diameter which is insertable in said vessel when stretched, whereby one end of a vessel from traumatic or surgical severance may be emplaced over each end of said cylinder, and fixedly positioned thereon, said cylinder being open to and permitting the flow of body fluids and being absorbable by living mammalian tissue.

* * * * *

EXHIBIT 10

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc.
a Massachusetts Corporation

Plaintiff,

v.

Arthrex, Inc.
a Delaware Corporation

Defendant.

Civil Action No. 04-12457 PBS

EXPERT REPORT OF ROBERT T. BURKS, M.D.

1. I am an orthopaedic surgeon with the University of Utah Orthopaedic Center. My office is at 590 Wakara Way, Salt Lake City, Utah 84108. I have been practicing for more than 23 years.

2. I received my M.D. from St. Louis University in 1974. I completed a residency in Orthopaedics at the University of California at San Diego in 1983. I completed a knee and sports medicine fellowship at Kaiser Permanente Hospital in San Diego in 1983, and sabbatical at Steadman Hawkins in Vail, Colorado in 1995

3. I am a Professor and Mary Scowcroft Peery Presidential Endowed Chair at the University of Utah Health Sciences Center. I am also the Director of Sports Medicine and Head Physician at the University of Utah. My curriculum vitae are attached as Exhibit 1.

4. My specialties include arthroscopy of the shoulder, knee and ankle, and ligament reconstruction. My research interests include patella stability, cartilage defects, tendon healing to bone.

5. I have reviewed Dr. Fenton's report and I understand he may provide testimony on certain subjects including human anatomy, surgical techniques and surgical devices. I may also provide testimony on these same subjects.

6. I may describe the characteristics of a surgical suture that are generally important to an orthopaedic surgeon. I may also describe the specific features of FiberWire that I find beneficial in my practice.

7. I have been using FiberWire suture in my surgical procedures since 2001. Most of my subjective use of FiberWire occurs during surgery and in the surgical environment, FiberWire is generally wet.

8. Sometime in February 2006, I was contacted by attorneys for Arthrex, Inc. and asked to conduct a tactile feel analysis as well as a knot tie-down analysis of coated and uncoated FiberWire suture. I agreed to conduct the analysis.

9. In March 2006, I received two samples of suture labeled "suture A" and "suture B." Each sample was on a spool and was approximately 3 meters in length. I was told by Arthrex's attorneys that one sample was coated US No. 2 FiberWire and that the other sample was uncoated US No. 2 FiberWire, however, I was not told which sample was coated and which was uncoated.

10. I took the sutures and cut them into some lengths that are appropriate for intraoperative tying and for intraoperative knot tying done arthroscopically. This allowed 5 strands from each spool.

11. I conducted a tactile feel analysis of both suture samples ("suture A" and "suture B"). During the analysis, I noticed that the sample labeled "suture A" generally felt smoother than "suture B." The difference between the two samples was even more pronounced when they were wet, which is how I am most accustomed to using FiberWire.

12. I also conducted a knot tie-down analysis on the two suture samples. I tied several surgeons knots and found that the knots slid easier on the sample labeled "suture A" as compared with the sample labeled "suture B." I felt less friction when sliding the knot on the sample labeled "suture A" as compared with the sample labeled "suture B." Here again, the difference between the two samples was most noticeable when they were wet, as I am accustomed to using FiberWire.

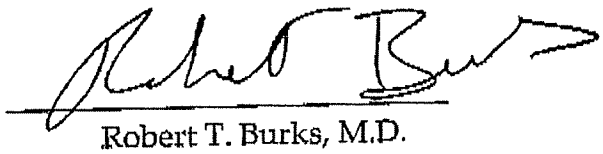
13. After conducting my analysis, I was informed that "suture A" was the coated FiberWire and "suture B" was the uncoated FiberWire.

14. If asked to testify at trial, I may use physical exhibits, as well as other demonstrative exhibits, which have not yet been developed.

15. Within the past four years, I have testified as an expert at deposition in connection with one other case: Philip D. Ceriani, M.D. v. Lonnie Paulos, M.D., and Simon Finger, M.D., et al, Case #: 030906702 (Civil 3rd District Court, Salt Lake City).

16. I am being compensated at a rate of $400 per hour.

Dated: March 24, 2006



Robert T. Burks, M.D.

EXHIBIT 11

UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF MASSACHUSETTS

-O-

DEPUY MITEK, INC., a Massachusetts Corporation,

Plaintiff,

-vs-

ARTHREX, INC., a Delaware Corporation, and PEARSALLS LTD., a Private Limited Company of the United Kingdom,

Defendants.

Civil Action No. 04-12457 PBS

EXPERT DEPOSITION OF:

ROBERT T. BURKS, M.D.

-O-

Location: Mariott University Hotel
Salt Lake City, Utah

Date: June 7, 2006
3:00 p.m.

Reporter: Denise Kirk, CSR/RPR

-O-

I described them.

Q. Okay, so why did you use the particular knots, then, that you used in the knot tie-down analysis?

46:51 A. I just tried to reproduce what I do in the operating room.

Q. In paragraph 11 in Exhibit 232 you state that suture A generally felt smoother than suture B. What do you mean by "generally"?

47:08 A. The differences between the sutures were subtle. I mean, they were not sharp, distinct. So I'm meaning that in comparing them, my take was that it was generally smoother.

Q. Were there any of the sutures in the

47:45 tactile feel analysis where you couldn't tell the difference between suture A and suture B?

A. It was not my intent at the time in looking at the sutures to compare each strand side to side. My intent was to look at sort of spool A and

18:13 spool B. So it was to get a feel of, in general, how do they feel between the two.

So I didn't take a strand and say is this one different? And is this one different? And go down through that five times, because I felt it was all the same suture.

whether those are coated or uncoated sutures?

MR. TAMBURO: Objection, calls for speculation.

A. I think gloves can make a difference, yeah.

Q. How do they make a difference? The difference between the sutures is more subtle, right, with gloves because you don't have the contact like you described earlier with the skin?

A. Yeah. Again, this is obviously a very subjective feel test. Some of that feel comes from how the suture feels and some of it comes from how you feel when you slide a knot. So we're not talking rocks and water as far as differences and so. . .

Q. How would you qualify the difference that you just observed, based on your test?

A. When you say "qualify" are you asking for like an amount?

Q. How would you characterize the difference between the sutures?

A. Well the difference is, I think, subtle and there's no doubt in my mind that I could line up, you know, a hundred sutures and have error where I would say, you know, I think this one is one way or the other and make a mistake.

EXHIBIT 12

US005312437A

United States Patent [19]

Hermes et al.

[11] Patent Number: 5,312,437

[45] Date of Patent: May 17, 1994

[54] **ABSORBABLE COATING COMPOSITION AND SUTURE COATED THEREWITH**

[75] Inventors: **Matthew E. Hermes**, Easton; **Donald S. Kaplan**, Weston; **Nagabhushanam Totakura**, Norwalk; **Steven L. Bennett**, Milford, all of Conn.

[73] Assignee: **United States Surgical Corporation**, Norwalk, Conn.

[21] Appl. No.: **896,856**

[22] Filed: **Jun. 12, 1992**

[51] **Int. Cl.**[5] **A61L 17/00**

[52] **U.S. Cl.** **606/230**; 606/231; 428/375; 428/378

[58] **Field of Search** 606/230, 231; 428/275, 428/375, 378; 525/354, 408

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,531,561	9/1970	Trehu	606/231
3,867,190	2/1975	Schmitt et al.	606/231
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4,027,676	6/1977	Mattei	606/230
4,043,344	8/1977	Landi et al.	606/230
4,047,533	9/1977	Perciaccante	606/230
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4,105,034	8/1978	Shalaby et al.	606/230
4,185,637	1/1980	Mattei	606/230
4,201,216	5/1980	Mattei	606/230
4,470,416	9/1984	Kafrawy et al.	606/230
4,624,256	11/1986	Messier et al.	606/230
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4,744,365	5/1988	Kaplan et al.	606/230
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Primary Examiner—Stephen C. Pellegrino
Assistant Examiner—Gary Jackson

[57] **ABSTRACT**

An absorbable composition for application to a surgical suture to improve the knot tie-down and/or knot security characteristics thereof is obtained from the reaction of a poly(oxypropylene) glycol and a lactide/glycolide copolymer, optionally, in the presence of an initiator and/or catalyst.

36 Claims, No Drawings

ABSORBABLE COATING COMPOSITION AND SUTURE COATED THEREWITH

BACKGROUND OF THE INVENTION

This invention relates to an absorbable coating composition for surgical sutures and to a coated surgical suture exhibiting improved knot tie-down and/or knot security characteristics.

Since monofilament synthetic absorbable suture materials are generally stiffer than their catgut or collagen counterparts, multifilament, e.g., braided or twisted, constructions have been employed in many instances for greater softness and flexibility. Multifilament sutures, however, exhibit a certain degree of undesirable roughness in what is generally referred to as knot tie-down performance, i.e., the ease or difficulty of sliding a knot into place down the suture. It has therefore become a common practice to coat sutures, particularly those of the multifilament variety, with compositions which improve their knot tie-down performance and perhaps one or more other properties of the sutures as well. Known suture coating compositions include those described in U.S. Pat. Nos. 3,867,190; 3,942,532; 4,027,676; 4,043,344; 4,047,533; 4,080,969, 4,105,034; 4,185,637, 4,201,216; 4,470,416; 4,624,256; 4,649,020; 4,716,203, 4,788,979; and, 4,857,602.

U.S. patent application Ser. No. 07/707,437, filed May 28, 1991 describes an absorbable composition for improving the knot tie-down properties of a suture, the composition being either a copolymer derived from the copolymerization of a low molecular weight poly(oxyethylene) glycol, glycolide monomer and a lactide monomer or a copolymer derived from the copolymerization of a low molecular weight polyalkylene glycol and a preformed copolymer of lactide and glycolide.

Notwithstanding the extensive research in attempting to improve the tie-down characteristics of surgical sutures, sutures having even further improved knot tie-down properties are still desirable.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide an absorbable coating composition for surgical sutures, particularly multifilament synthetic sutures.

Another object of this invention is to provide a coated surgical suture exhibiting improved knot tie-down characteristics.

Still another object of the present invention is to provide an absorbable coated synthetic suture exhibiting improved knot tie-down characteristics under both wet and dry conditions.

A further object of this invention is to provide an absorbable coated synthetic suture exhibiting improved knot security characteristics.

These and other objects are achieved herein by providing an absorbable coating composition comprising the product obtained by reacting a mixture of poly(oxypropylene) glycol and a lactide/glycolide copolymer in the presence or absence of an initiator. Coated sutures having improved knot tie-down characteristics under dry and wet conditions as well as improved knot security characteristics are provided by depositing a coating of the afore-described composition on the suture.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The preferred poly(oxypropylene) glycols used in preparing the suture coating composition of this invention possess molecular weights ranging from about 400 to about 6,000 and more preferably from about 1,000 to about 4,000 and viscosities of from about 70 to about 2,000 cp, preferably from about 150 to about 1,200 cp and, more preferably, from about 900 to about 1200 cp. Suitable poly(oxypropylene) glycols include those of the Pluracol (BASF-Wyandotte), Voranol (Dow), Poly G (Olin), Polylite (Reichhold), Thanol (Texaco) and Niax (Union Carbide) series.

The preferred lactide/glycolide copolymers are made from about 90 to about 65 mole percent lactide, from about 10 to about 35 mole percent glycolide and from 0 to about 5 mole percent of one or more additional monomers copolymerizable therewith such as p-dioxanone, ϵ-caprolactone, etc. Copolymers of this type and their preparation are known, e.g., from U.S. Pat. Nos. 2,668,162; 2,703,316; 3,297,033; 3,620,218; 3,636,956; 3,736,646; 3,773,919,; 3,797,499; 3,839,297; 3,867,190; 3,982,543; 4,273,920; and, 4,523,591.

More preferred lactide/glycolide copolymers for use in preparing the coating composition herein are the 85–70 mole percent lactide/15–30 mole percent glycolide copolymers described in U.S. Pat. No. 4,523,591, the contents of which are incorporated by reference herein. The copolymers are advantageously prepared with L-lactide and possess a glass transition temperature of at least about 54° C. when measured by differential scanning calorimetry at 20° C./min and an inherent viscosity of at least about 0.9 when measured in chloroform at a concentration of 0.25 g/dl. A particularly preferred lactide/glycolide copolymer is prepared with about 18 mole percent lactide and about 82 mole percent glycolide.

The absorbable coating composition herein is prepared by reacting the poly(oxypropylene) glycol(s) with the lactide/glycolide copolymer(s), generally in the presence of an esterification catalyst such as stannous chloride, stannous octoate, etc., and, optionally, an initiator. Suitable initiators include glycols such as ethylene glycol, propylene glycol, diethylene glycol and dipropylene glycol. A preferred glycol, diethylene glycol, is advantageously employed at a level of from about 0.01 to about 0.1 weight percent, and preferably at a level of from about 0.02 to about 0.5 weight percent, of the reaction medium. The weight ratio of poly(oxypropylene) glycol to lactide/glycolide copolymer can vary from about 4:1 to about 1:4 and preferably from about 2:1 to about 1:2, respectively. Typically, the reaction is carried out in an inert atmosphere, e.g., nitrogen, at temperatures, for example, of from about 125° to about 200° C., and preferably from about 150° to about 160° C. When employing a lactide/glycolide copolymer possessing an inherent viscosity of at least about 0.9, it is preferred to carry out the reaction until the inherent viscosity of the coating composition has fallen below about 0.9, and more preferably below about 0.5, when measured in chloroform at a concentration of 0.25 g/dl. Reaction periods of from about 10 to about 24 hours are generally sufficient to accomplish this.

The absorbable coating composition of the present invention is non-toxic and physiologically inert. It can be applied to the surface of a suture in the form of a solution and/or dispersion in a volatile carrier such as

methylene chloride or acetone. Solidification of the coating on the suture surface occurs upon evaporation of the carrier.

The coating composition can be applied to a suture by any suitable process, e.g., passing the suture through a solution of the coating composition, past a brush or other coating solution applicator, or past one or more spray nozzles dispensing the coating solution. The suture wetted with the coating solution is subsequently passed through or held in a drying oven for a time and at a temperature sufficient to volatilize and drive off the solvent.

The coating composition can, if desired, contain one or more other components, e.g., dyes, antibiotics, antiseptics, growth factors, anesthetics, anti-inflammatory agents, etc.

While the coating composition herein can be applied to any type of suture, it is essentially intended for application to a braided suture, a preferred type of which is disclosed in U.S. Pat. No. 5,019,093, the contents of which are incorporated by reference herein. The amount of coating composition applied to a braided suture will vary depending upon the structure of the suture, e.g., the number of filaments, tightness of braid or twist, the size of the suture and its composition.

The coating composition herein can be used for both "unfilled" as well as "filled" sutures, the latter designating braided bioabsorbable sutures containing a storage stabilizing material as disclosed in U.S. Pat. Nos. 5,037,429 or 5,051,272, the contents of which are incorporated by reference herein. For an "unfilled" suture, the coating composition can be applied at a level of from about 0.5 to about 4 weight percent or more and preferably from about 1 to about 3 weight percent. Advantageously, the coating composition is applied to the suture prior to application of the storage stabilizing material. For a filled suture, the amount of applied coating composition can range from about 0.2 to as much as about 3 weight percent or more and preferably from about 0.5 to about 2 weight percent. As a practical matter, it is generally preferred to apply the minimum amount of coating composition consistent with good tie-down performance. This level of coating add-on can be readily determined for any particular suture coating system employing routine experimental procedures.

In the case of an unfilled or filled braided suture, prior to application of the coating composition, it can be advantageous to calender the suture in order to improve the uniformity with which the coating composition is laid down upon the suture surface. A calendering operation can also be beneficial when carried out on a coated suture where the suture is to be filled with a storage stabilizing material. In this case, calendering will tend to break up the coating facilitating penetration of the interior spaces of the suture by the storage stabilizing material.

A preferred method for calendering a braided suture and an apparatus for carrying out the method are disclosed in copending U.S. patent application Ser. No. 07/652,939, filed Feb. 8, 1991, the contents of which are incorporated by reference herein. In accordance with Ser. No. 07/652,939, calendering of a braided suture is achieved by applying a compressive force to the suture in a first line or direction generally transverse to the longitudinal direction of the suture, the compressive force being of sufficient magnitude as to flatten the suture in a direction orthogonal to the direction in which the compressive force is applied. Preferably, a second application of compressive force is applied to the suture in a direction generally transverse to that of the first compressive force and transverse to the longitudinal direction of the suture. The second compressive force is substantially equal in magnitude to the first compressive force so that the suture returns to its original cross-sectional configuration.

The apparatus for implementing the foregoing calendering method includes at least one pair of rollers which are biased towards each other to apply a compressive force to the suture as the suture passes between them. Optionally, a second pair of rollers is provided which is oriented at an angle (preferably 90°) to the first pair of rollers and transverse to the longitudinal direction of the suture. Following passage between both the first and second pair of rollers, the suture will have been alternately compressed, or flattened, in a first direction and thereafter in a second direction at an angle to the first direction.

The following examples are illustrative of the absorbable coating composition of this invention, its preparation and sutures coated therewith.

EXAMPLE 1

This example illustrates the preparation of an absorbable suture coating composition in accordance with the invention.

A poly(oxypropylene) glycol of 4,000 average molecular weight (nominal) and a viscosity of from 900–1200 cp, 677±1 g, was introduced into a reactor equipped with a stirrer. Following a minimum 6 hour period of drying the poly(oxypropylene) glycol in a stream of anhydrous nitrogen gas, a previously dried lactide/glycolide copolymer containing 82 mole percent lactide and 18 mole percent glycolide and an inherent viscosity of at least 0.9 when measured in chloroform at a concentration of 0.25 g/dl (prepared as disclosed in U.S. Pat. No. 4,523,591 referred to above), 1,323±1 g, was introduced into the reactor. The reactor, which was maintained under a blanket of nitrogen gas, was heated to a temperature of 155°–170° C. Thereafter, 0.4±0.05 g stannous octoate catalyst and 0.4±0.05 g diethylene glycol initiator were added to the reactor, the latter being stirred at a rate of 55–60 rpm. Following a reaction period of 20–25 hours, the reaction product was recovered and residual reactant(s) removed therefrom at elevated temperature and under a pressure not exceeding 10 Torr, the temperature profile being as follows:

1. Ramped to 80° C. at 5° C./hr.
2. Soaked at 80° C. for 1 hr.
3. Ramped to 125° C. at 2.5° C./hr.
4. Soaked at 125° C. for 1–48 hrs.
5. Cooled to ≦30° C.

The reaction product, which had an inherent viscosity below 0.5 when measured in chloroform at a concentration of 0.25 g/dl, was used as the coating composition in Examples 2 and 3 which follow.

EXAMPLE 2: COMPARATIVE EXAMPLES 1–3

Suture knot security for a coated suture in accordance with this invention (Example 2) and three known types of suture (Comparative Examples 1–3) was evaluated in divided canine fascia (linea alba) using a standard surgeon's knot.

The sutures of Example 2 were size 0 synthetic absorbable braided sutures constructed in accordance with U.S. Pat. No. 5,019,093, and coated with approxi-

mately 2.6 percent by weight of suture with the coating composition of Example 1 using the apparatus of Ser. No. 07/652,929, supra, by passing the suture through calender rolls, past a coating head to deposit the desired amount of coating composition in solvent and evaporating the solvent in a drying oven. Thereafter, the coated suture was calendered and filled with approximately 10 weight percent lycerin/calcium lactate in accordance with U.S. Pat. No. 5,037,429 using the calendering and filling apparatus of Ser. No. 07/652,939.

The sutures of Comparative Example 1 were size 0 Vicryl ® synthetic absorbable braided sutures from Ethicon Inc. The sutures are believed to be coated with a copolymer of glycolide/lactide with calcium stearate.

The sutures of Comparative Example 2 were size 0 sutures constructed in accordance with U.S. Pat. No. 5,019,093, coated with approximately 1.4 percent by weight of suture with a 50:50 weight ratio copolymer of glycolide/lactide (18:82 mole percent) and poly(oxyethylene) glycol as disclosed in pending U.S. patent application Ser. No. 07/707,437, U.S. Pat. No. 5,123,912, referred to above and filled with approximately 10 weight percent glycerin/calcium lactate in accordance with U.S. Pat. No. 5,037,429. The sutures of Comparative Example 3 were coated and filled in substantially the same manner as in Example 2 employing the same equipment.

The sutures of Comparative Example 3 were the same as the sutures of Comparative Example 2 except that the coating was applied at approximately 3.0 percent by weight of suture.

The knot was configured as a hand tie (two right over left throws plus one left over right throw). The sutures were evaluated in normal abdominal fascia as well as thicker fascia toward the pubis The results of the testing are set forth below as the number of sutures which held without slipping per total number of sutures tied.

	Normal Fascia	Heavy Fascia
Example 2	4:4	4:6
Comparative Example 1	4:8	3:4
Comparative Example 2	1:3	0:2
Comparative Example 3	1:6	—

These results demonstrate the superior knot security characteristics conferred by the suture coating composition of this invention compared to that obtained with known coating compositions.

EXAMPLE 3; COMPARATIVE EXAMPLES 4–6

Knot run-down for a coated suture in accordance with this invention (Example 3) and three known types of suture (Comparative Examples 4–6) was evaluated by forming a hand tied square knot (right over left throw plus left over right throw) approximately 1 cm from the fascial edge of canine tissue and then running the knot down tightly around the fascial edge.

The sutures of Example 3 were size 3/0 sutures identical in all other respects to the sutures of Example 2 and the sutures of Comparative Examples 4, 5 and 6 were size 3/0 sutures identical in all other respects to the sutures of Comparative Examples 1, 2 and 3, respectively The results of the testing are set forth below as the number of sutures which ran down and the total number of tries.

	Knot Run Down
Example 3	4:6
Comparative Example 4	6:6
Comparative Example 5	3:6
Comparative Example 6	2:6

The test results show that sutures coated with the coating composition of the present invention demonstrate superior run-down characteristics compared to sutures of identical construction which have been coated with the composition disclosed in pending U.S. patent application Ser. No. 07/707,437, filed May 28, 1991, referred to above. Moreover, the properties of the coated suture compare favorably with those of a commercial suture of comparable size.

What is claimed is:

1. A suture coated with a coating composition comprising the product obtained by reacting a mixture of poly(oxypropylene) glycol and lactide/glycolide copolymer.

2. The suture of claim **1** wherein the poly(oxypropylene) glycol possesses a molecular weight of from about 400 to about 6,000.

3. The suture of claim **1** wherein the poly(oxypropylene) glycol possesses a molecular weight of from about 1,000 to about 4,000.

4. The suture of claim **1** wherein the lactide/ glycolide copolymer is prepared with L-lactide.

5. The suture of claim **1** wherein the lactide/glycolide copolymer contains from about 90 to about 65 mole percent lactide and from about 10 to about 35 mole percent glycolide.

6. The suture of claim **1** wherein the lactide/glycolide copolymer contains from about 85 to about 70 mole percent lactide and from about 15 to about 30 mole percent glycolide.

7. The suture of claim **1** wherein the lactide/glycolide copolymer prior to reaction with the poly(oxypropylene) glycol possesses a glass transition temperature of at least about 54° C. when measured by differential scanning calorimetry at 20° C./min and an inherent viscosity of at least about 0.9 when measured in chloroform at a concentration of 0.25 g/dl.

8. The suture of claim **7** wherein the composition following reaction possesses an inherent viscosity of less than about 0.9 when measured in chloroform at a concentration of 0.25 g.dl.

9. The suture of claim **7** wherein the composition following reaction possesses an inherent viscosity of less than about 0.5 when measured in chloroform at a concentration of 0.25 g/dl.

10. The suture of claim **1** wherein the weight ratio of poly(oxypropylene) glycol to lactide/glycolide copolymer is from about 4:1 to about 1:4.

11. The suture of claim **1** wherein the weight ratio of poly(oxypropylene) glycol to lactide/glycolide copolymer is from about 2:1 to about 1:2.

12. The suture of claim **1** wherein the composition following reaction possesses in inherent viscosity of less than about 0.9 when measured in chloroform at a concentration of 0.25 g/dl.

13. The suture of claim **1** wherein the composition following reaction possesses an inherent viscosity of less than about 0.5 when measured in chloroform at a concentration of 0.25 g/dl.

14. The suture of claim 1 wherein the poly(oxypropylene) glycol is reacted with the lactide/glycolide copolymer in the presence of an initiator.

15. The suture of claim 14 wherein the initiator is a glycol.

16. The suture of claim 15 wherein the glycol is diethylene glycol.

17. The suture of claim 1 wherein the suture is a synthetic multifilament suture.

18. The suture of claim 1 wherein the suture is an absorbable synthetic multifilament suture.

19. The suture of claim 1 exhibiting improved knot tie-down and/or knot security characteristics compared with the knot tie-down and/or knot security characteristics of the same suture coated with an equivalent amount of an absorbable composition obtained by reacting a poly(oxyethylene) glycol with a mixture of lactide and glycolide and/or lactide/glycolide copolymer.

20. A method of improving the knot tie-down and/or knot security characteristics of a suture which comprises coating the suture with an absorbable composition comprising the product obtained by reacting a mixture of poly(oxypropylene) glycol and lactide/-glycolide copolymer.

21. The method of claim 20 wherein the poly(oxypropylene) glycol possesses a molecular weight of from about 400 to about 6,000.

22. The method of claim 20 wherein the poly(oxypropylene) glycol possesses a molecular weight of from about 1,000 to about 4,000.

23. The method of claim 20 wherein the lactide/-glycolide copolymer is prepared with L-lactide.

24. The method of claim 20 wherein the lactide/-glycolide copolymer contains from about 90 to about 65 mole percent lactide and from about 10 to about 35 mole percent glycolide.

25. The method of claim 20 wherein the lactide/-glycolide copolymer contains from about 85 to about 70 mole percent lactide and from about 15 to about 30 mole percent glycolide.

26. The method of claim 20 wherein the lactide/-glycolide copolymer prior to reaction with the poly(oxypropylene) glycol possesses a glass transition temperature of at least about 54° C. when measured by differential scanning calorimetry at 20° C./min and an inherent viscosity of at least about 0.9 when measured in chloroform at a concentration of 0.25 g/dl.

27. The method of claim 26 wherein the composition following reaction possesses an inherent viscosity of less than about 0.9 when measured in chloroform at a concentration of 0.25 g.dl.

28. The method of claim 26 wherein the composition following reaction possesses an inherent viscosity of less than about 0.5 when measured in chloroform at a concentration of 0.25 g/dl.

29. The method of claim 20 wherein the weight ratio of poly(oxypropylene) glycol to lactide/glycolide copolymer is from about 4:1 to about 1:4.

30. The method of claim 20 wherein the weight ratio of poly(oxypropylene) glycol to lactide/glycolide copolymer is from about 2:1 to about 1:2.

31. The method of claim 20 wherein the poly(oxypropylene) glycol is reacted with the lactide/glycolide copolymer in the presence of an initiator.

32. The suture of claim 31 the initiator is a glycol.

33. The suture of claim 32 wherein the glycol is diethylene glycol.

34. The method of claim 20 wherein the suture is a synthetic multifilament suture.

35. The method of claim 20 wherein the suture is an absorbable synthetic multifilament suture.

36. The method of claim 20 wherein the resulting coated suture exhibits improved knot tie-down and/or knot security characteristics compared with the knot tie-down and/or knot security characteristics of the same suture coated with an equivalent amount of an absorbable composition obtained by reacting a poly(oxyethylene) glycol with a mixture of lactide and glycolide and/or lactide/glycolide copolymer.

* * * * *

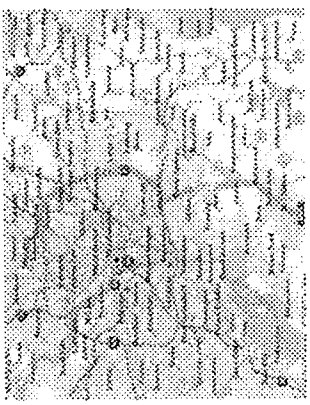

Exhibit 13

United States Patent [19]

Mattei et al.

[11] **Patent Number: 4,532,929**

[45] **Date of Patent: Aug. 6, 1985**

[54] **DRY COATING OF SURGICAL FILAMENTS**

[75] Inventors: **Frank V. Mattei**, Piscataway; **Donald W. Regula**, Flagtown, both of N.J.

[73] Assignee: **Ethicon, Inc.**, Somerville, N.J.

[21] Appl. No.: **633,759**

[22] Filed: **Jul. 23, 1984**

[51] **Int. Cl.**[3] **A61L 17/00**

[52] **U.S. Cl.** **128/335.5**; 427/2; 428/263; 428/378

[58] **Field of Search** 128/335, 335.5; 428/263, 378; 427/2

[56] References Cited

U.S. PATENT DOCUMENTS

3,478,140	11/1969	Kronenthal et al.	128/335.5
4,027,676	6/1977	Mattei	128/335.5
4,047,533	9/1977	Perciaccante et al.	128/335.5
4,105,034	8/1978	Shalaby et al.	128/335.5
4,201,216	5/1980	Mattei	128/335.5

Primary Examiner—Jacqueline V. Howard
Attorney, Agent, or Firm—Charles J. Metz

[57] ABSTRACT

Braided or monofilament surgical filaments are coated with dry, powdered, substantially water-insoluble, absorbable salt of a C_6 or higher fatty acid, such as calcium stearate.

20 Claims, No Drawings

DRY COATING OF SURGICAL FILAMENTS

TECHNICAL FIELD

This invention relates to a dry, absorbable composition useful as a coating and lubricating finish for surgical filaments, and to a method for using said composition. More particularly, this invention relates to a means for improving the tie-down properties of absorbable and non-absorbable monofilament surgical filaments as well as multifilament surgical filaments by coating them with a dry, absorbable lubricating composition.

BACKGROUND ART

Suture materials and other surgical filaments such as ligatures are generally classified as either absorbable or non-absorbable, with each type of suture material being preferred for certain applications. Absorbable suture materials are preferred for internal wound repair in which the sewn tissues will hold together without suture reinforcement after healing and in which a nonabsorbed suture may promote tissue irritation or other adverse bodily reaction over an extended period of time. Suture materials are considered to be absorbable if they disappear from the sewn tissue within about a year after surgery, but many absorbable suture materials disappear within shorter periods.

The earliest available absorbable suture materials were surgical gut and extruded collagenous materials. More recently, absorbable sutures derived from synthetic polymers have been developed which are strong, dimensionally uniform, and storage stable in the dry state. Typical of such polymers are lactide homopolymers and copolymers of lactide and glycolide such as those disclosed in U.S. Pat. No. 3,636,956, and glycolide homopolymers such as those disclosed in U.S. Pat. No. 3,565,869.

Monofilament synthetic absorbable suture materials are generally stiffer than their multifilament surgical gut or collagen counterparts, and synthetic absorbable sutures are therefore usually employed in a multifilament, braided construction in order to provide the suture with the desired degree of softness and flexibility. Such multifilament sutures exhibit a certain degree of undesirable roughness or "grabbiness" in what has been termed their "tie-down" performance, i.e., the ease or difficulty of sliding a knot down the suture into place, or the ease of snugging a square knot in place.

Multifilament nonabsorbable sutures such as braided sutures of polyethylene terephthalate, for example, can be improved with respect to tie-down performance by coating the external surface of the suture with solid particles of polytetrafluorethylene and a binder resin as disclosed in U.S. Pat. No. 3,527,650. This procedure, however, is undesirable as applied to absorbable sutures because polytetrafluoroethylene is nonabsorbable and sutures coated therewith would leave a polymer residue in the sewn tissue, after the suture had been absorbed.

Multifilament, nonabsorbable sutures can also be improved with respect to tie-down performance by coating them with a linear polyester having a molecular weight between about 1,000 and about 15,000 and at least two carbon atoms between the ester linkages in the polymer chain as disclosed in U.S. Pat. No. 3,942,532.

U.S. Pat. No. 3,297,033 discloses that the synthetic absorbable sutures described therein may be coated with conventional suture coating materials such as a silicone or beeswax in order to modify the handling or absorption rate of the sutures. These coating materials are not readily absorbable, however, and will accordingly leave an undesirable residue in the tissue after the suture itself is absorbed.

Many other compounds have been proposed as treating agents to improve the lubricity and handling of both natural and synthetic filaments. U.S. Pat. No. 3,896,841 describes the treatment of collagen sutures with a hygroscopic agent and lubricant to provide a suture which permanently retains at least 10 percent by weight moisture. Sutures so treated are reported to have increased suppleness and reduced drag when passing through tissue. Fatty compounds and derivatives of fatty compounds are suggested as useful lubricating agents for such collagen sutures.

U.S. Pat. No. 3,982,543 discloses that multifilament, absorbable sutures may be lubricated/coated with a copolymer of lactide and glycolide in order to reduce the capillarity of the suture, and that sutures so treated are reported to have improved run down.

Because of the nature of surgical procedures, sutures and ligatures are generally exposed to body fluids or passes one or more times through moist tissue before tying, and an effective suture coating composition ideally provides wet tie-down characteristics substantially equivalent to those of the dry suture.

U.S. Pat. No. 4,143,423 discloses coating surgical applicances with a gloving agent or lubricant comprising a water soluble nontoxic alkali metal compound such as sodium bicarbonate. The compound may be coated as a powder by dusting or from an aqueous solution. Water soluble compounds would not, however, be suitable as lubricants for surgical sutures due to the nature of surgical procedures. Thus, the lubricant powders would be dissolved prematurely.

U.S. Pat. No. 4,201,216, issued May 6, 1980, to Frank V. Mattei, discloses as a coating for sutures, particularly synthetic absorbable multifilament sutures, an absorbable composition comprising a film-forming polymer and a substantially water-insoluble salt of a C_6 or a higher fatty acid. The coating is preferably applied to the suture from a solvent solution to provide a final coating add-on of from about 2 to 10 percent by weight of the sutures. In accordance with the teachings of said U.S. Pat. No. 4,201,216, the film-forming polymer is preferably a copolymer of lactide and glycolide, while the fatty acid salt is preferably a calcium salt of a C_6 to C_{22} fatty acid. The ratio of polymer to fatty acid salt in the coating composition may be within the range of about 1:4 to 4:1 parts by weight. The coating is wholly absorbable and is particularly useful for improving the dry and wet tie-down smoothness of braided sutures prepared from homopolymers and copolymers of lactide and glycolide, and other absorbable polymers. The patent discloses that where the compositions of the suture and the film former are identical, and in other instances where the suture material may be subject to some surface dissolution and/or surface swelling or softening by reason of the action of the film former solvent thereon, there may be a gradual transition between the substrate composition and the coating composition rather than a sharp interface between them. There may also be some weakening of the suture accompanying the application of such coating compositions.

It is an object of this invention to provide an improved method for coating monofilament sutures, as

well as multi-filament sutures of braided, twisted or covered construction, with a coating that improves the tie-down properties of such monofilament or multifilament sutures. It is a further object of this invention to provide a wholly absorbable coated synthetic monofilament or multifilament suture having improved and substantially equal dry and wet knot tie-down properties. It is yet a further object of this invention to provide such a wholly absorbable coated synthetic monofilament or multifilament suture having improved tie-down properties at least as desirable as those of sutures prepared in accordance with the teaching of U.S. Pat. No. 4,201,216, but having a substantially lower coating weight than that of the sutures of said U.S. Pat. No. 4,201,216, thus tie-down is improved by the minimal application of a safe material, such application being accomplished without using any organic solvents. The appearance and other esthetic attributes of the suture are only minimally affected, if at all, by the low level of add-on of the dry lubricating composition of the invention.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the invention, there is provided as a coating for surgical filaments such as sutures, and ligatures, particularly synthetic absorbable monofilament surgical filaments, an absorbable composition comprising a dry, finely powdered, substantially water insoluble salt of a C_6 or higher fatty acid. The coating may be applied on continuous lengths of monofilament or braid, using a series of powdered soft brushes followed by clean, soft wiping brushes to remove excess coating powder, or using other powder coating techniques that are known to the art, to provide a final coating add-on of below about 0.25 percent, and preferably below about 0.15 percent, by weight of the filament. The coating may also be applied to the filament manually by pulling the filament through fingers that had been powdered with the coating salt, e.g., calcium stearate, followed by pulling several times through clean fingers to remove any visible signs of the coating powder.

The fatty acid salt is preferably a calcium salt of a C_6 to C_{22} fatty acid. The coating is particularly useful for improving the dry and wet tie-down smoothness of monofilament sutures, such as those prepared from homopolymers and copolymers of p-dioxanone, polyolefins such as polypropylene, certain polyesters, and the like, as well as braided sutures prepared from homopolymers and copolymers of lactide or glycolide and other absorbable polymers, polyethylene terephthalate, silk, and the like.

The fatty acid salts useful in the coating powder compositions of the invention include the calcium, magnesium, barium, aluminum, and zinc salts of C_6 and higher fatty acids, particularly those having from about 12 to 22 carbon atoms, and mixtures thereof. The calcium salts of stearic, palmitic and oleic acids are particularly preferred for use in the invention. Mixtures of these salts may offer advantages in certain applications.

The amount of coating composition applied to the suture, or the coating add-on, will vary depending upon the construction of the suture, e.g., the number of filaments and tightness of braid or twist. In general, the coating composition applied to a suture will constitute up to about 0.25 percent by weight of the coated suture, and preferably up to about 0.15 percent by weight of the suture. As a practical matter, and for reasons of economy and general performance, it is generally preferred to apply the minimum amount of coating composition consistent with good tie-down performance, and this level of add-on is readily determined experimentally for any particular suture-coating system. Usually, the add-on will be at least about 0.02 weight percent, based on suture weight.

The improvement in tie-down properties imparted to sutures and ligatures may be determined semiquantitatively and subjectively by comparing the tie-down smoothness of coated and uncoated filaments during the act of tying down a single throw knot. Such comparisons are preferably made on both wet and dry filaments since many filaments materials have different tie-down properties when tested wet or dry. Tie-down roughness is graded from 0 to 10, with 0 being comparable to a rough filament and 10 indicating no detectable roughness.

Tie-down properties are evaluated dry after the strands of suture or ligature have been conditioned for at least 2 days in a vacuum drying oven at room temperature and 100 microns absolute pressure, and wet after being immersed in water at 25° C. for 1 minute. Values above 4 are considered acceptable, while values of 7 or higher are comparable to conventional silicone coated silk and are considered fully satisfactory.

The tie-down roughness test is carried out as follows:

The calibration standards for the test are uncoated poly(glycolide-co-lactide) braid, size 2/0, which is arbitrarily assigned a 0 rating, and size 2/0 braided poly(ethylene terephthalate) having a coating of polytetrafluoroethylene, which is assigned a 10 rating. A 24–36 inch strand of the material being tested is looped under a stationary bar, and a single throw know (overhand knot) is formed between the two free ends, near the ends. The two ends are grasped firmly in the hands and the ends are arranged so that the knot has its loops evenly spread out. Using 1–2 pounds of tension, the knot is caused to slide down at a moderate rate, with an even pull, until it comes to rest on the bar. After calibrating the strands for some 10–15 minutes with the two standards, the smoothness of tie-down is judged for the test samples, using the 0–10 scale. Usually, some 3–5 tie-downs are done on each strand, and about 4 strands are done per sample. For wet tie-down, the test is carried out immediately upon removal from the water. Only about 3 to 4 wet tie-downs are done on each strand, since the strand begins to dry out immediately upon removal from the water, and after 3 or 4 tests, is no longer wet. An average is taken of all the evaluations. While the test is subjective, and obviously operator-dependent, experiences has shown that different persons carrying out the test will get about the same results (i.e., the trends and differences between samples will be the same), even though the specific numbers obtained may not be exactly the same.

The following examples are provided to further illustrate and demonstrate the method and product of the invention. Unless otherwise stated, all parts and percentages are by weight.

EXAMPLE 1

Dry, powdered (100 percent smaller than 21 microns, 50 percent smaller than 8.5 microns) calcium stearate (in the form of a commercial food grade product consisting of about $\frac{1}{3}$ C_{16} and $\frac{2}{3}$ C_{18} fatty acid, with small amounts of C_{14} and C_{22} fatty acids) was applied as follows to size

1 dyed poly-p-dioxanone monofilament which had been scoured in acetone for three hours and then dried. The operator's fingers were powdered with the calcium stearate and the strands then individually pulled through the fingers 4–8 times so as to obtain a thorough and intimate coating. After removing the stearate from the fingers, the strands were pulled through clean fingers several more times to remove any visible signs of stearate.

EXAMPLE 2

The foregoing procedure was repeated using the monofilaments and fatty acid salt coating powders identified in Table I. The tie-down properties of the strands were then evaluated using the heretofore described semi-quantitative smoothness-of-tie-down tests, with the results set forth in Table I. The sterilized samples were sterilized either by ethylene oxide (EO) or by gamma irradiation from a cobalt-60 source.

TABLE I

Monofilament		% Add-on, 10 six foot strands	Smoothness of Tie-Down Ratings Based on 0–10 Subjective Scale					
			Dry			Wet		
			Unsterilized/Sterilized			Unsterilized/Sterilized		
Size 0, dyed poly-p-dioxanone monofilament	Uncoated control		3.5	4	(EO)	7.5	7.5	(EO)
Size 0, dyed poly-p-dioxanone monofilament	Calcium stearate	0.041	10	10	"	10	10	"
Size 0, dyed poly-p-dioxanone monofilament	Calcium palmitate		10	9.5	"	9.5	9.5	"
Size 0, dyed poly-p-dioxanone monofilament	Calcium laurate		10	10	"	10	10	"
Size 0, dyed poly-p-dioxanone monofilament	Calcium oleate		3	3	"	8	8	"
Size 0, dyed poly-p-dioxanone monofilament	Calcium undecylenate		10	10	"	9.5	9.5	"
Size 0, dyed poly-p-dioxanone monofilament	Zinc stearate	0.15	9	9.5	"	9.5	9	"
Size 0, dyed poly-p-dioxanone monofilament	Magnesium stearate		10	10	"	9	9.5	"
Size 0, dyed poly-p-dioxanone monofilament	Magnesium myristate		9.5	9.5	"	9.5	9.5	"
Size 0, dyed poly-p-dioxanone monofilament	Zinc undecylate		10	10	"	9.5	10	"
Size 0, dyed poly[tetramethylene terephthalate-CO—(2-octadecenyl) succinate] monofilament (U.S. Pat. No. 4,388,296)	Uncoated control		2	1.5	(COBALT)	2	2	(COBALT)
	Calcium stearate		9	8	"	9	9	"
	Calcium palmitate		8	8	"	9	8.5	"
	Calcium laurate		6	5.5	"	2.5	4	"
	Zinc stearate		8.5	8.5	"	8.5	9	"
Size 0 Dyed Polypropylene monofilament	Uncoated control		2	1.5	(EO)	2	2	(EO)
Size 0 Dyed Polypropylene monofilament	Calcium stearate	0.06	9	9	"	9.5	9.5	"
Size 0 Dyed Polypropylene monofilament	Calcium palmitate		9	9	"	9	9	"
Size 0 Dyed Polypropylene monofilament	Calcium laurate		9.5	9.5	"	9.5	9	"
Size 0 Dyed Polypropylene monofilament	Zinc stearate	0.126	9.5	9.5	"	9	9	"
Size 2/0 scoured nylon[1] monofilament	Uncoated Control		6.5	—		7	—	
	Calcium stearate	—	10	—		9.5	—	

[1]Soaked in acetone for 3 hours at room temperature.

As is apparent from the above results, the dry coating of the invention is effective for improving the tie-down characteristics of a variety of surgical filaments such as sutures and ligatures using various salts of fatty acids. In the tests reported in Table I, only the calcium oleate coating of the poly-(p-dioxanone) monofilament suture showed no improvement in the dry test. Even this suture showed slight improvement in the wet tie-down test, although the results were not as good as for the other salts.

It may be readily appreciated that the coating may be used with good results on absorbable monofilament and multifilament sutures and ligatures as well as on nonabsorbable monofilament and multifilament sutures and ligatures.

Nonabsorbable sutures and ligatures such as cotton, linen, silk, polypropylene, and polyester are sometimes coated with nonabsorbable compositions. Polyolefins are usually of monofilament construction while cotton, linen, silk, and polyester are usually of braided, twisted, or covered multifilament construction. While there is usually no requirement that coatings on such sutures be absorbable, the composition of the invention may, nevertheless, be used as a finish for nonabsorbable sutures if desired. The only suture material that has been tried and found not to be improved by the invention is unscoured nylon monofilament. That is because unscoured nylon already has such good tie-down properties that any improvement that might be imparted by the invention is not detectable by the semi-quantitative subjective test used.

EXAMPLE 3

Twenty strands of size 0 undyed polyester (polyethylene terephthalate) braid, in three-foot lengths, were coated with dry calcium stearate powder by the procedure described in Example 1, above. The add-on level for the twenty strands was 1.5 weight percent (this was probably much higher than the add-on would be in a

commercial process, with a more efficient cleaning operation after the coating). Wet tie-down was 8½ (average of 4 strands), while the dry tie-down was 9 (average of 4 strands), using the same test for smoothness of tie-down described above. The uncoated controls were rated at 1 for both dry and wet. The appearance of the coated strands was excellent; they appeared to the naked eye to be uncoated.

What is claimed is:

1. A synthetic surgical filament having improved and substantially equal dry and wet tie-down properties, said surgical filament having been coated with from about 0.02 to 0.25 percent by weight of a composition consisting essentially of a dry, powdered, substantially water-insoluble, absorbable salt of a C_6 or higher fatty acid.

2. A surgical filament of claim 1, wherein said higher fatty acid is selected from the group consisting of C_{12} to C_{22} fatty acids and mixtures thereof.

3. A surgical filament of claim 1, wherein the fatty acid salt is a salt of calcium, magnesium, barium, aluminum, or zinc.

4. A surgical filament of claim 2, wherein the fatty acid salt is a salt of calcium or magnesium.

5. A surgical filament of claim 4, wherein the fatty acid comprises a mixture of stearic and palmitic acid.

6. A surgical filament of claim 5, wherein the fatty acid salt comprises a mixture of calcium palmitate and calcium stearate.

7. A surgical filament of claim 1, coated with from about 0.02 to 0.15 percent of the said mixture.

8. A surgical filament of claim 1, which is comprised of homopolymers or copolymers of lactide or glycolide.

9. A surgical filament of claim 8, wherein said surgical filament is comprised of a copolymer of 10 weight percent lactide and 90 weight percent glycolide.

10. A surgical filament of claim 9, which is a braided multifilament suture or ligature.

11. A surgical filament of claim 1, which comprises a homopolymer or a copolymer of p-dioxanone.

12. A surgical filament of claim 1, which is a monofilament suture or ligature.

13. A surgical filament of claim 11, which is a monofilament suture or ligature.

14. A surgical filament of claim 1 which is composed of a polymer selected from the group consisting of the polyolefins and the polyesters.

15. A method for imparting improving and substantially equal dry and wet tiedown properties to a surgical filament which comprises applying to the surface of said surgical filament in the form of a dry powder a water-insoluble, absorbable salt of a C_6 or higher fatty acid, and thereafter removing from the surface of said surgical filament excess said powder by rubbing said surface in intimate contact with a relatively powder free, nonabrasive surface until no powder is visible to the naked eye on said surgical filament surface.

16. The method of claim 15, wherein the fatty acid salt is the salt of calcium, magnesium, barium, aluminum, or zinc.

17. The method of claim 16, wherein said higher fatty acid is selected from the group consisting of C_{12} to C_{22} fatty acids and mixtures thereof.

18. The method of claim 15, wherein said surgical filament is an absorbable synthetic polymer selected from the group consisting of homopolymers and copolymers of lactide or glycolide.

19. The method of claim 15, wherein said surgical filament is a nonabsorbable synthetic polymer selected from the group consisting of the polyolefins and the polyesters.

20. The method of claim 16 wherein said surgical filament is a homopolymer or a copolymer of p-dioxanone.

* * * * *

Exhibit 14

IN THE COURT OF CHANCERY OF THE STATE OF DELAWARE
IN AND FOR THE NEW CASTLE COUNTY

DEPUY MITEK, INC., a Massachusetts Corporation, Plaintiff,	)	Civil Action
v.	)	No. 04-12457 PBS
ARTHREX, INC., a Delaware Corporation, Defendant.	)	

CONFIDENTIAL - NON-PATENT ATTORNEY'S EYES ONLY

deposition of:

BRIAN HALLETT

HIGHLY CONFIDENTIAL

taken at:
The Castle Hotel
Castle Green
Taunton
Somerset
UNITED KINGDOM

on
11th January 2006

goes to a line yarn?
A It takes off any excess coating.
Q After that?
A Yes.
Q Now, the oven process that we have here, I think you referred to it as drying and the curing?
A That's correct.
Q Is the drying process here a technical curing process, or is it just drying the yarn?
MR. TAMBURO: Object to the form of the question.
A It does.
MR. BONELLA: What do you mean by that?
A Well, it is actually acting as a -- it dries out the coating, it burns off any excess chemicals as it comes through the bath, and it acts as actually purifies the new coating.
Q Purifies it? What do you mean by that?
A Without speculation, I would just imagine it is -- fills in any gaps and makes sure it is completely covered.
Q Is there material change that takes place during the -- is there any change that takes place on the coating during the drying process?
MR. TAMBURO: Objection to the form of the

Exhibit 15

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. **a Massachusetts Corporation** **Plaintiff,** **v.** **Arthrex, Inc.** **a Delaware Corporation** **Defendant.**	)	**Civil No. 04-12457 PBS**

DePuy Mitek's Supplemental Responses To Arthrex, Inc.'s First Set of Interrogatories

DePuy Mitek sets forth both its original responses and its supplemental responses below. Each supplemental response is intended to incorporate in its entirety the original response, including any objections.

Interrogatory No. 2

For each claim of the '446 Patent identified in response to Interrogatory No. 1, state the basis for DePuy Mitek's (as defined above) contention of infringement separately with respect to each and every product of Arthrex accused of infringement, including a claim chart explaining DePuy Mitek's contention as to how each element of each claim being asserted is met by each specific Arthrex product, whether such alleged infringement is literal or under the doctrine of equivalents, identify any and all documents on which DePuy Mitek relies to support its response to this interrogatory and identify the three individuals currently and/or formerly within DePuy Mitek's employ who are believed to be the most knowledgeable with respect to the subject matter of this interrogatory.

Response to Interrogatory No. 2

DePuy Mitek objects to this interrogatory to the extent that it demands information that is immune from discovery on the basis of the attorney-client privilege, the work-product doctrine, or Rule 26(b)(4)(B) immunity.

DePuy Mitek further objects to this interrogatory as premature because discovery has just begun, and DePuy Mitek has not yet received sufficient information from Arthrex to answer this interrogatory with the specificity that Arthrex seeks.

FiberWire marketing materials, FiberWire is described as being strong and handleable, just as the claimed sutures. Thus, there would be infringement under the doctrine of equivalents.

DePuy Mitek further states that the 446 Patent, its prosecution history, FiberWire's Design File Histories, and FiberWire manufacturing documents are relevant documents to its response.

Interrogatory No. 6

For each claim identified in response to Interrogatory No. 1, identify: (a) the chronology of the research from conception to the date of reduction to practice of the recited subject matter and indicate whether actual or constructive; (b) all events relating to such conception and reduction to practice; (c) the person or persons who were involved in such conception and reduction to practice; (d) the person or persons other than the inventor(s) who are most knowledgeable about the facts concerning conception and reduction to practice; and (e) all documents concerning such conception and reduction to practice.

Response to Interrogatory No. 6

DePuy Mitek objects to this interrogatory to the extent that it demands information that is immune from discovery on the basis of the attorney-client privilege, the work-product doctrine, or Rule 26(b)(4)(B) immunity.

DePuy Mitek objects to this interrogatory as premature because discovery has just begun. Further, DePuy Mitek does not in the first instance have the burden to prove a date of conception and reduction to practice until Arthrex comes forward with an invalidity defense that DePuy Mitek needs to rebut. In this regard, DePuy Mitek notes that Arthrex has not fully responded to DePuy Mitek's discovery requests on this matter.

DePuy Mitek objects to this interrogatory as ambiguous and unintelligible because based on its improper definition of DePuy Mitek. It demands an answer from companies and persons other than DePuy Mitek. DePuy Mitek is the only plaintiff in this action and therefore, no other company or person is answering this interrogatory.

DePuy Mitek objects to the interrogatory including the phrases "the chronology;" "all events relating to such conception and reduction to practice;" "the person or persons who were involved;" and "all documents concerning such conception and reduction to practice" as vague, ambiguous, overbroad, unduly burdensome, and demanding information that is not reasonably calculated to lead to the discovery of admissible evidence or relevant to any pled claim or defense.

DePuy Mitek further objects to this interrogatory as demanding discovery of information that is not within its possession, custody, or control.

Subject to its general and specific objections and without waiving them, DePuy Mitek states that the inventions claimed in the 446 Patent were developed by Alastair Hunter, Arthur Taylor, Jr. and Mark Steckel while they were employed by Ethicon, Inc. They are the persons most knowledgeable about the invention. Because the patent is presumed valid, DePuy Mitek does not in the first instance have the burden to show a conception and reduction to practice in the absence of an invalidity defense putting those matters in issue. Arthrex has not set forth with any specificity such a defense. Notwithstanding, as presently advised, the invention was conceived by and was actually reduced to practice well before the February 19, 1992 filing date. DePuy Mitek identifies the inventor's lab notebooks and other research and development information that is in the possession, custody and control of Ethicon, Inc. as describing the conception and actual reduction to practice.

Supplemental Response to Interrogatory No. 6

Subject to its objections, based on information that is currently in its possession, and with the understanding that its investigation is still on-going, DePuy Mitek further states that the claimed inventions were conceived at least as early as June 6, 1988 and reduced to practice at least as early as February 2, 1989 at Ethicon, Inc. Dr. Mark Steckel, Alistar Hunter, and Arthur Taylor were involved in the conception of the claimed invention. The inventors, and other persons working at their direction, including Mr. Crawford Britt, were involved in the reduction to practice of the claimed invention. Dr. Steckel reported to Allison Skinner when the invention was reduced to practice.

At least as early as June 6, 1988, the inventors conceived of the idea of a suture having a heterogeneous braid as claimed in the 446 Patent. For example, Dr. Steckel's laboratory notebook describes the concept of a "braided suture constructed of two or more fiber types designed to realize the beneficial properties of each polymer." Dr. Steckel's notebook further states that the "composites to be evaluated include PET/PTFE" and "PET/PP." As explained, the idea that the PET/PTFE and PET/PP combinations of yarns could be blended by "carrier blending" or "dividing the carriers into two sets with yarn A residing on one set and yarn B on the other" had been developed. Dr. Steckel's notebook further describes various composite

braids that were evaluated. They included a PET/PTFE braid and PET/PP braids that were carrier blended as denoted by "CB." Dr. Steckel's notebook also describes the construction and evaluation of a braid that was formed with a carrier braider and had a braid of PTFE and PET.

Documents describing the chronology of the research and development include the documents bearing bates numbers DMI002269-2678 and DMI002199-2268.

Interrogatory No. 10

Identify all third parties (i.e., any person or entity not a person to this action) contacted (in writing, in person, telephonically, electronically, or otherwise) by or on behalf of DePuy Mitek (as defined above) concerning the '446 Patent and/or any of Arthrex's surgical suture products, including but not limited to Arthrex's FiberWire® suture products, and for each third party identified, identify the person(s) who made such contact(s), the date(s) of such contact(s), all persons involved with the decision to make such contact(s) and the substance of such contact(s) as related in any way to the '446 Patent and/or such Arthrex products, and identify any and all documents referring or relating to such contact(s).

Response to Interrogatory No. 10

DePuy Mitek objects to this interrogatory to the extent that it demands information that is immune from discovery on the basis of the attorney-client privilege, the work-product doctrine, or Rule 26(b)(4)(B) immunity.

DePuy Mitek objects to this interrogatory as overbroad, unduly burdensome, vague, ambiguous, and unintelligible because of its improper definition of DePuy Mitek. It demands an answer from companies and persons other than DePuy Mitek. DePuy Mitek is the only plaintiff in this action and therefore, no other company or person is answering this interrogatory.

DePuy Mitek objects to the interrogatory including the phrases "Arthrex's surgical suture products;" "any and all documents referring or relating to such contact(s)" and "and the substance of such contact(s) as related in any way to the '446 Patent and/or such Arthrex products" as vague, ambiguous, overbroad, unintelligible, unduly burdensome, and demanding information that is not reasonably calculated to lead to the discovery of admissible evidence or relevant to any pled claim or defense.

Rick Gilson, John Grange, and Meghan Scanlon of DePuy Mitek, Inc. were contacted for information regarding this lawsuit and information requested in interrogatories 3-6.

Other persons at DePuy Mitek, Inc. and Ethicon, Inc. were contacted to collect and gather information but they would be too numerous to mention.

Dated: July 1, 2005

DEPUY MITEK, INC.,

By its attorneys,

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Lynn A. Malinoski
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617-439-2000

CERTIFICATE OF SERVICE

I certify that the foregoing **DePuy Mitek's Supplemental Responses to Arthrex's, Inc.'s First Set of Interrogatories** was served by facsimile and overnight mail on July 1, 2005 on the following:

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Christopher Weld, Jr.
Todd & Weld LLP
28 State Street, 31st Floor
Boston, MA 02109
Fax: (617) 227-5777

Dated: July 1, 2005

Lynn Malinoski

Exhibit 16

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. **a Massachusetts Corporation** **Plaintiff,** **v.** **Arthrex, Inc.** **a Delaware Corporation and** **Pearsalls Ltd.** **a Private Limited Company of** **the United Kingdom** **Defendants.**	)	**Civil No. 04-12457 PBS**

DePuy Mitek's Supplemental Responses To Arthrex, Inc.'s Interrogatories

DePuy Mitek sets forth both its original responses and its supplemental responses below. Each supplemental response is intended to incorporate in its entirety the original response, including any objections.

Interrogatory No. 2

For each claim of the '446 Patent identified in response to Interrogatory No. 1, state the basis for DePuy Mitek's (as defined above) contention of infringement separately with respect to each and every product of Arthrex accused of infringement, including a claim chart explaining DePuy Mitek's contention as to how each element of each claim being asserted is met by each specific Arthrex product, whether such alleged infringement is literal or under the doctrine of equivalents, identify any and all documents on which DePuy Mitek relies to support its response to this interrogatory and identify the three individuals currently and/or formerly within DePuy Mitek's employ who are believed to be the most knowledgeable with respect to the subject matter of this interrogatory.

Response to Interrogatory No. 2

DePuy Mitek objects to this interrogatory to the extent that it demands information that is immune from discovery on the basis of the attorney-client privilege, the work-product doctrine, or Rule 26(b)(4)(B) immunity.

DePuy Mitek further objects to this interrogatory as premature because discovery has just begun, and DePuy Mitek has not yet received sufficient information from Arthrex to answer this interrogatory with the specificity that Arthrex seeks.

Interrogatory No. 6

For each claim identified in response to Interrogatory No. 1, identify: (a) the chronology of the research from conception to the date of reduction to practice of the recited subject matter and indicate whether actual or constructive; (b) all events relating to such conception and reduction to practice; (c) the person or persons who were involved in such conception and reduction to practice; (d) the person or persons other than the inventor(s) who are most knowledgeable about the facts concerning conception and reduction to practice; and (e) all documents concerning such conception and reduction to practice.

Response to Interrogatory No. 6

DePuy Mitek objects to this interrogatory to the extent that it demands information that is immune from discovery on the basis of the attorney-client privilege, the work-product doctrine, or Rule 26(b)(4)(B) immunity.

DePuy Mitek objects to this interrogatory as premature because discovery has just begun. Further, DePuy Mitek does not in the first instance have the burden to prove a date of conception and reduction to practice until Arthrex comes forward with an invalidity defense that DePuy Mitek needs to rebut. In this regard, DePuy Mitek notes that Arthrex has not fully responded to DePuy Mitek's discovery requests on this matter.

DePuy Mitek objects to this interrogatory as ambiguous and unintelligible because based on its improper definition of DePuy Mitek. It demands an answer from companies and persons other than DePuy Mitek. DePuy Mitek is the only plaintiff in this action and therefore, no other company or person is answering this interrogatory.

DePuy Mitek objects to the interrogatory including the phrases "the chronology;" "all events relating to such conception and reduction to practice;" "the person or persons who were involved;" and "all documents concerning such conception and reduction to practice" as vague, ambiguous, overbroad, unduly burdensome, and demanding information that is not reasonably calculated to lead to the discovery of admissible evidence or relevant to any pled claim or defense.

DePuy Mitek further objects to this interrogatory as demanding discovery of information that is not within its possession, custody, or control.

Subject to its general and specific objections and without waiving them, DePuy Mitek states that the inventions claimed in the 446 Patent were developed by Alastair Hunter, Arthur Taylor, Jr. and Mark Steckel while they were employed by Ethicon, Inc. They are the persons most knowledgeable about the invention. Because the patent is presumed valid, DePuy Mitek does not in the first instance have the burden to show a conception and reduction to practice in the absence of an invalidity defense putting those matters in issue. Arthrex has not set forth with any specificity such a defense. Notwithstanding, as presently advised, the invention was conceived by and was actually reduced to practice well before the February 19, 1992 filing date. DePuy Mitek identifies the inventor's lab notebooks and other research and development

information that are in the possession, custody and control of Ethicon, Inc. as describing the conception and actual reduction to practice.

Second Supplemental Response to Interrogatory No. 6

Subject to its objections, Mitek further supplements its response to interrogatory no. 6 as follows.

Dr. Steckel and D. Jamiolkowski's depositions and the exhibits to their depositions provide further evidence of conception and reduction to practice and the chronology of development of the claimed invention. For example, Dr. Steckel testified that the invention was conceived at least as early as the first half of 1988. Further, Dr. Steckel testified that he or others working with him or at his direction made a heterogeneous, carrier braid of PET and PTFE yarns at least as early as June 1988. This braid is described in his laboratory notebook. Dr. Jamiolkowski also testified to a conception of the invention and making of a braid at least as early as June 1988. The further chronology of the development of the invention, diligence, and the events associated with the development can be found in their deposition transcripts and exhibits.

Interrogatory No. 8

Identify actual gross sales figures (U.S. dollars), actual and anticipated profit margins, profit and loss and DePuy Mitek's (as defined above) costs, on a monthly basis, associated with the manufacture and sale of each product identified in response to Interrogatory No. 3 and identify any projections of future sales, anticipated profit margins, anticipated profit and loss and anticipated costs associated with the manufacture and sale of such product, including any reviews, studies and/or market analyses conducted in connection with such projections, including the date(s), author(s) and recipient(s) of such reviews, studies and/or market analyses and identify and all documents that embody or refer to such actual and projected sales figures, profits and costs and identify the three persons currently, and/or formerly within DePuy Mitek's employ who are believed to be the most knowledgeable with respect to the subject matter of this interrogatory.

DMI95312-95316; DMI95317-95321; DMI95322-95327; DMI095332-95341; DMI95158-95172; DMI94180-94245 under FED. R. CIV. P. 33(d).

Dated: February 24, 2006

DEPUY MITEK, INC.,

By its attorneys,

Dianne B. Elderkin
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617-439-2000

CERTIFICATE OF SERVICE

I certify that the foregoing DePuy Mitck's Supplemental Responses To Arthrex, Inc.'s Interrogatories was served by facsimile on February 24, 2006 on the following:

Charles W. Saber
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Todd & Weld LLP
28 State Street, 31st Floor
Boston, MA 02109
Fax: (617) 227-5777

Dated: February 24, 2006

Michael Bonella

Exhibit 17

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

C.A. No. 04-12457 PBS

----------x

DePUY MITEK, INC.,

A Massachusetts Corporation,

Plaintiff,

v.

ARTHREX INC.,

A Delaware Corporation,

Defendants.

----------x

ORIGINAL

DEPOSITION OF MATTHEW GOODWIN

New Brunswick, New Jersey

January 17, 2006

Reported by:

MARY F. BOWMAN, RPR, CRR

JOB NO.: SE 173

GOODWIN

A. Can I rule it out?

Q. Yes.

A. I don't remember when I met with Mr. Steckel.

Q. So you have no idea?

A. No.

Q. What happened next after you met with Mr. Steckel?

A. I don't remember.

Q. Well, eventually a patent application was filed, right?

A. Correct.

Q. You have no recollection what happened in between the time you met Mr. Steckel and the filing of the patent application?

A. No.

Q. Do you recall if a draft was provided to Mr. Steckel for review before the application was filed in 19 -- on February 19, 1992?

A. I don't recollect preparing a draft.

Q. So what is your recollection?

A. Simply that I met with him to discuss this invention.

Q. And you have no recollection of a

GOODWIN

draft?

A. No.

Q. Do you have any recollection of any writing with respect to this patent application prior to February 19, 1992 when it was filed?

A. No, I don't.

MS. MALINOSKI: Vague.

A. I don't have any recollection of the drafting process here.

Q. If a draft did exist, where would it be?

MS. MALINOSKI: Objection, assumes facts not in evidence, improper hypothetical.

A. If a draft did exist, where would it be?

Q. Yes, sir.

A. I don't know.

Q. Do you normally keep drafts in your files?

A. No.

Q. What do you normally do with drafts?

A. I discard them.

Q. So even if a draft was prepared in

Exhibit 18

Johnson & Johnson

Office Of
GENERAL COUNSEL

NEW BRUNSWICK, N.J.

February 3, 1992

SUBJECT: ETH 782 - Entitled "Sterilized Heterogeneous Braids"

B. Schwartz

Barbara, I wanted to let you know that I have been unable to complete this application for filing. It relates to composite braid sutures.

I sent a substantially complete draft, including examples and drawings, to Mark Steckel for review and comment. I then received comments from Chuck Fritz, and I understand that Mark received comments from the remaining coinventors.

I left two voice mail messages for Mark during the first week of January, requesting that he call me to discuss changes to the draft. Dennis Jamiolkowski also requested Mark to contact me. Our requests have gone unanswered.

I'm very sorry that this seems to be a continuing problem. Unfortunately, there is nothing I can do without full cooperation from Mark.

Matthew S. Goodwin

MSG/sc
cc: C. Fritz

CONFIDENTIAL - OUTSIDE
ATTORNEYS EYES ONLY

DePuy Mitek, Inc. v. Arthrex, Inc.
C.A. No.04-12457 PBS
DMI095016

1 129-216

ETHICON, INC.
a Johnson & Johnson company
P.O. BOX 151
SOMERVILLE • NEW JERSEY • 08876-0151

February 10, 1992

Mr. M. Steckel

cc: Mr. M. Banik
Mr. M. Goodwin

Mark, the attached memo has been of great concern to me. I would appreciate your responding to Matt Goodwin's request, and communicating to me your timing with respect to this response.

As far as I am concerned, the work involved is extremely important to the suture business, and given your history with this subject, requires your immediate attention. We are already long past due in filing this patent.

Please contact me as quickly as possible regarding this matter.

Barbara Schwartz, Ph.D.

pak

Exhibit 19

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

C.A. No. 04-12457 PBS

----------x

DePUY MITEK, INC.,

A Massachusetts Corporation,

Plaintiff,

v.

ARTHREX INC.,

A Delaware Corporation,

Defendants.

----------x

* * *CONFIDENTIAL* * *

DEPOSITION OF ILYA KOYFMAN

Somerset, New Jersey

February 22, 2006

Reported by:

MARY F. BOWMAN, RPR, CRR

JOB NO.: SE232

KOYFMAN - Confidential

Q. Is he still --

A. No, he is not, and I lost touch with him, so I'm not sure where he is.

Q. Do you know when he left U.S. Surgical?

A. I don't know exact time, but he left after I left. So it was maybe a year or two years after I left.

Q. I guess we were talking a little bit about the timing of this work. Do you see that the patent, do you see the date the patent was filed? Four five lines down, February 3, 1992.

A. Um-hm.

Q. Using that as a reference date, do you know, compared to that date, when the work was done that led to this patent?

A. I think that's, as I recall, the dates I mentioned to you, perhaps '91, perhaps -- no, I don't know. Around that time.

Q. So the work you were doing you had started about a year before this, give or take?

A. Possibly, yes.

Q. I am sorry?

A. I don't -- I'm not sure exactly but

KOYFMAN - Confidential

that's my recollection.

Q. It started about a year before?

A. Yes.

Q. I think you said year, year and a half in response to my earlier question.

MR. BONELLA: Object to form.

Q. Is the length of the time of the project. So I am trying to get a sense of when it occurred?

A. I don't remember the dates anymore, but --

Q. Sure, I appreciate that.

A. I think around that time and maybe a year or so.

Q. The work was done about a year, during the year before this when the patent was filed?

MR. BONELLA: Object to the form, mischaracterizes the testimony.

MR. SABER: Let me finish the question.

MR. BONELLA: Sorry.

Q. Is it correct that to the best of your recollection, that the work that led to this patent was done during the year prior to the

Exhibit 20

US005318575A

United States Patent [19]

Chesterfield et al.

[11] Patent Number: 5,318,575

[45] Date of Patent: Jun. 7, 1994

[54] METHOD OF USING A SURGICAL REPAIR SUTURE PRODUCT

[75] Inventors: Michael P. Chesterfield, Norwalk; Ilya Koyfman, Orange, both of Conn.

[73] Assignee: United States Surgical Corporation, Norwalk, Conn.

[21] Appl. No.: 829,423

[22] Filed: Feb. 3, 1992

[51] Int. Cl.[5] A61B 17/00

[52] U.S. Cl. 606/151; 606/228; 606/231; 128/898; 623/13

[58] Field of Search 606/228, 231, 151; 623/13; 128/898

[56] References Cited

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Primary Examiner—Stephen C. Pellegrino
Assistant Examiner—J. A. Schmidt

[57] ABSTRACT

Textile surgical articles are disclosed which are constructed in whole or in part from high tenacity low elongation fibers such as ultra-high molecular weight extended chain polyethylene high tenacity fibers. The products may be braided, woven or knitted, such as braided tapes, hollow braids and spiroid braids. The high tenacity low elongation fibers provide structures having greatly increased strength and decreased elongation, a combination of properties which is uniquely applicable and superior for repairing body tissue. The products may be plasma treated to reduce slip.

12 Claims, 2 Drawing Sheets

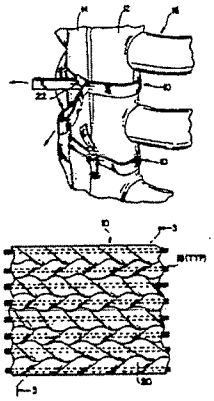

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FIG. 1

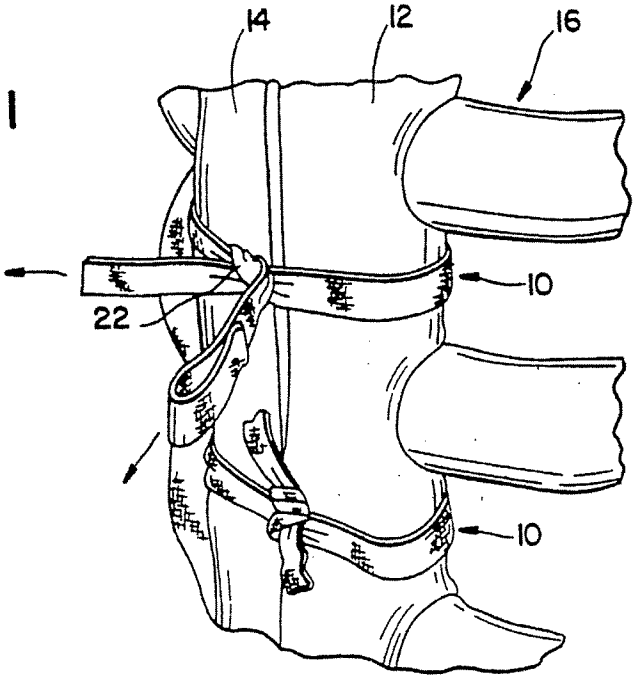

FIG. 2

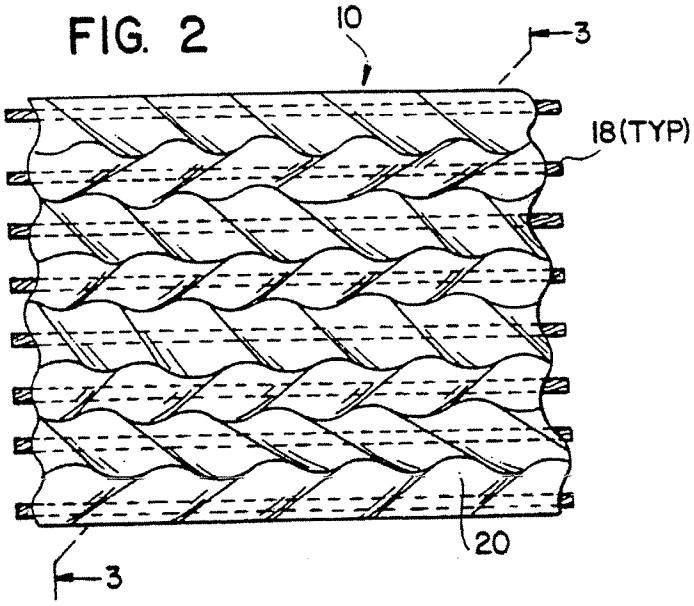

FIG. 3

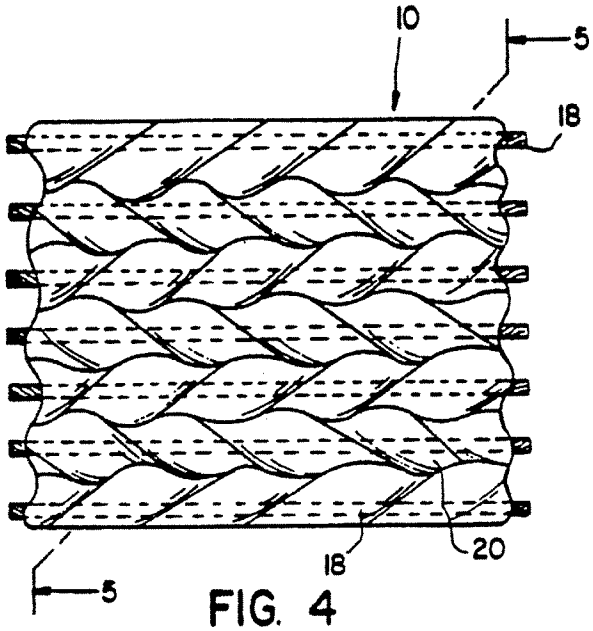

FIG. 4

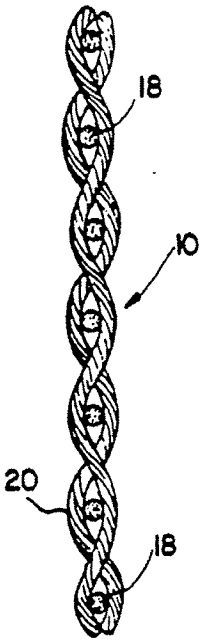

FIG. 5

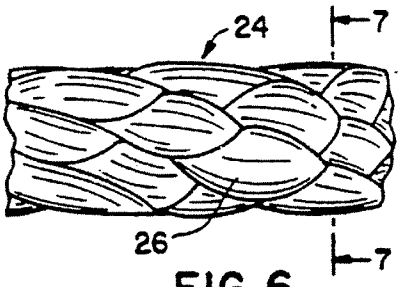

FIG. 6

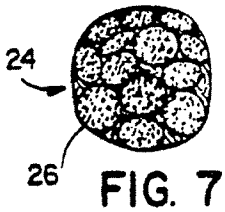

FIG. 7

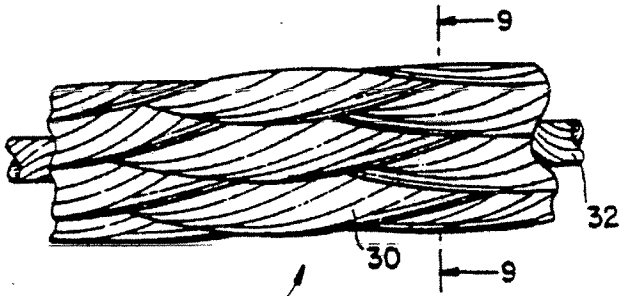

FIG. 8

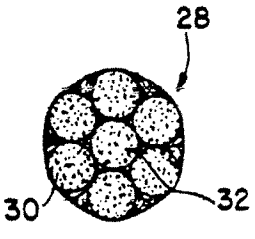

FIG. 9

METHOD OF USING A SURGICAL REPAIR SUTURE PRODUCT

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to suture products for surgical repair of body tissue. In particular, the invention is directed to reinforced surgical repair products for repairing the human sternum after surgery.

2. Background of the Prior Art

Presently there are many known products for repairing human body tissue in areas where a repair may be required either as a result of an injury or during or after surgery. In particular, it is well known to utilize suture products in the form of elongated strands to repair human body tissue as well as utilizing two-part fasteners or metal staples for attaching body tissue after portions have been removed during surgery.

For example, sutures intended for repairing soft body tissue are usually constructed of a plurality of filaments and applied to the tissue with any number of surgical needles. More recently, a certain amount of emphasis as been placed upon repairing surgical bone utilizing an elongated surgical product either in the form of a flat band or in the form of a strand having the construction similar to a suture by simply utilizing a needle to penetrate the bone to apply the repair product to the bone in a manner which physically retains the separated bone portions together to promote permanent healing. One such example is disclosed in U.S. Pat. No. 4,535,764 to Ebert which relates to a surgical bone tie having a needle connected to one end of a band such that the band may be looped and arranged to be appropriately looped around the bone portions requiring repair.

U.S. Pat. No. 4,813,416 relates to a band assembly and method for sternum closing with which the sternum halves are brought to abutting closure utilizing a band having a needle at one end to facilitate looping the band in position to retain the sternum portions in adjacent butting contacting relation.

Numerous other products have been used to retain bone portions together to promote healing while numerous suture products have been used to retain soft tissue to retain healing.

While many attempts have been made to provide such products little emphasis has been applied to the physical strength characteristics of the components which form the actual suture or band product in order to provide the surgeon with precision control on the product. Moreover, control is required on the tissue to which the product is applied in a manner which will promote healing of the tissue, yet will not cause unnecessary cutting of the tissue when force is applied to the product and the force is in turn applied to the tissue.

A particularly desirable product for accomplishing these goals would preferably display substantial strength without significant elongation to facilitate retaining the tissue portions together. In the case of attaching separate bone portions of the sternum together after open heart surgery for example, it has been necessary to utilize metal wire filaments by looping the wire filaments around the sternum portions and actually twisting the filament ends together to form an attachment. The metal wire displayed sufficient strength to retain the bone portions together without elongation. However, the wire represented a relatively sharp non-absorbable foreign body which remains embedded within the body tissue and thus presents a potential source of infection or other complications as a result of its presence within the body. Moreover, the relatively sharp characteristics of the wire present a danger of cutting into the bone during the application to the sternum. The sharp wire also presents a hazard to the surgeon and operating room personnel in that the wire may penetrate surgical gloves and cut the surgeon or attendant personnel, thereby creating a potential site for transmission of disease.

While utilization of wire sutures has been used and accepted during open heart surgery there remains room for improvement in the products used for strapping the split sternum portions together. Desirably, it would be best to provide a known metallic product which not only provides the strength to elongation characteristics of the metal sutures but which may be utilized to form a tying product for soft as well as hard tissue, in a manner which will minimize the dangers of cutting of the tissue in the surrounding areas. The present invention is directed to such a product.

SUMMARY OF THE INVENTION

In accordance with the present invention, textile surgical articles are disclosed which are made in whole or in part from high tenacity low elongation fibers such as ultra high molecular weight extended chain polyethylene high tenacity fibers. One such fiber is Spectra yarn from Allied Signal Corp. The products may be braided, woven or knitted, although braided tape, hollow braids and spiroid braids are preferred. The high tenacity low elongation fibers provide structures having greatly increased strength and decreased elongation.

In one embodiment, braided tapes are made from Spectra yarn. In an alternative embodiment braided tapes are made with Spectra runners and bioabsorbable, Dacron polyester and/or nylon fill yarns.

Further alternative embodiments include tubular braided structures having a core made in whole or in part from high tenacity low elongation fibers or spiroid braided structures made in whole or in part from high tenacity low elongation fibers.

In a preferred method of the invention, a braided tape reinforced with ultra-high molecular weight high tenacity fibers is used to join a divided sternum by tying, or other appropriate means. The tape has a very high strength, preferably equal to or greater than 35 kg. straight pull and more preferably greater than about 50 kg. straight pull, and low elongation at break, preferably below about 20%, more preferably below about 10 to 15%, and most preferably below about 5%.

BRIEF DESCRIPTION OF THE DRAWINGS

Preferred embodiments of the invention are described hereinbelow wherein:

FIG. 1 is a perspective view of a portion of a split human sternum illustrating one application of the present invention for retaining the split portions together to promote healing;

FIG. 2 is an enlarged view of the suture product shown in FIG. 1 illustrating one embodiment wherein the elongated product is a flat braided member and contains at least eight reinforcing filaments extending along the length;

FIG. 3 is a cross-sectional view taken along lines 3—3 of FIG. 2.;

FIG. 4 is an enlarged view of an alternative embodiment of the suture repair product of FIG. 2 wherein the elongated braided product contains at least seven reinforcing filaments extending along the length;

FIG. 5 is a cross-sectional view taken along lines 5—5 of FIG. 4;

FIG. 6 is a view of an alternative embodiment of the suture repair product wherein the elongated member is a spiroid braided member having a generally circular cross-section containing at least one elongated reinforcing member;

FIG. 7 is a cross-sectional view taken along lines 7—7 of FIG. 6;

FIG. 8 is a view of another alternative embodiment of the suture repair product wherein the elongated product is a hollow braided member having a generally circular cross-section and contains at least one elongated reinforcing member extending centrally thereof along the length; and

FIG. 9 is a cross-sectional view taken along lines 9—9 of FIG. 8.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring initially to FIG. 1 there is illustrated a sternum closure ribbon 10 constructed according to the present invention and positioned to retain portions 12,14 of a human sternum 16 together. The band 10 is preferably a braided product as shown in FIGS. 2 and 4 having a plurality of elongated filamentary reinforcing members of ultra high molecular weight polyethylene fibers. The fibers may be plasma treated to reduce slip characteristics of the yarn, if desired. In particular, such fibers as extended chain polyethylene high tenacity fibers (ECPE) marketed under the trademark SPECTRA ® by Allied-Signal Technologies, Petersburg, Va. 23804 are preferred as reinforcing members provided in the product of the present invention. SPECTRA 1000 yarn is suitable. These extended chain fibers exhibit a molecular weight generally between about 1 million to about 5 million but also may be as low as 500,000. They exhibit a very substantial degree of crystalline orientation (95–99%) and crystalline content (60–85%). As a result the fibers exhibit strengths from about 375 kpsi (thousands of pounds per square inch) to about 560 kpsi and tensile moduli of from about 15 msi (millions of pounds per square inch) to about 30 msi. The significant strength and stability of these fibers are caused by the high degree of molecular orientation. Moreover, since the fibers can be provided as multifilament or monofilament fibers which can be braided, woven, knitted or otherwise processed to form a textile product it will be readily appreciated that any number of reinforced textile products may be provided similar to the band 10 shown in the drawings, but with numerous alternative applications as will be described hereinbelow.

Referring now to FIG. 2, the band 10 shown in FIG. 1 is shown in greater detail as an elongated flat braided textile product having a plurality of high molecular weight fibers 18 extending along the length of the band.

The elongated fibers 18 are preferably made of ECPE marketed under the SPECTRA ® trademark and are surrounded by braided fibers 20 which may be of the bioabsorbable type. For example, fibers 20 may be made of any suitable bioabsorbable polymeric material such as polymers or copolymers of glycolide, lactide, p-dioxanone, polyester, polyamino acids and the like as disclosed in U.S. Pat. Nos. 2,668,162; 3,297,033; 3,636,956; 3,736,646; and 3,839,297. The number of reinforcing filaments 18 included in the braided band 10 shown in FIG. 2 is optional as is the specific construction of the band. For example, as seen in FIG. 4, there is an example of an alternative braided band construction having seven reinforcing filaments 18 of high molecular weight, high strength fibers of the type shown in FIG. 2. Furthermore, as seen in FIG. 7, there is an alternative elongated embodiment of spiroid braided construction of generally circular cross-section and comprised of one or more elongated filaments 26 of high molecular weight, high strength, with the remainder of the braid being of bioabsorbable filamentary materials to form a braided rope-like construction of generally circular cross-sectional configuration as shown in FIG. 7. Alternatively the braided product 22 may be constructed entirely of such high molecular weight, high strength, elongated filaments 24. Braid constructions having a circular cross-section are described in U.S. Pat. Nos. 3,565,077 and 5,019,093. Any number of combinations of bioabsorbable yarns, filamentary or otherwise, and/or non-absorbable, and high strength filaments are contemplated, depending upon the intended application.

In FIGS. 8 and 9 there is shown a hollow braid construction 28 having a sheath constructed of bio-absorbable yarns 30 and having a core 32 of high molecular weight, high strength filament. Any number of alternative combinations of 0 to 100% absorbable filamentary or otherwise,. and/or non-absorbable yarns and high strength filaments are contemplated depending upon the intended application.

It will be appreciated that in addition to the examples which follow hereinbelow, numerous alternative textile constructions may be incorporated into the present invention to form a reinforced band for attaching body tissue such as a soft tissue or bone tissue without suffering from the disadvantages from presently known materials. For example, it is conceivable within the scope of the present invention to provide a woven structure containing a plurality of elongated high strength filaments 18 in the warp direction wherein the filler yarns are of a suitable bioabsorbable material such as polymers or copolymers of glycolide, lactide, p-dioxanone, polyester, polyamino acids and the like, or with fill yarns of a nonabsorbable material such as Dacron polyester or nylon. Likewise, knitted structures may be strengthened by reinforcement with high tenacity fibers. It will be appreciated that in each of the embodiments discussed herein the strength characteristics of the high tenacity, low elongation fibers 18 will provide the substantial force carrying capability to the elongate product while the fibers 20 surrounding the high strength filaments will provide the necessary structural support to the main fibers for forming the product. The surrounding fibers will also define the "hand" or "feel" of the band.

Accordingly, it is possible in one application to position the reinforced structure 10 about the split portions 13,14 of the human sternum 16 as shown in FIG. 1 whereby substantial force may be applied to the band by tying the band either by a knot 22 shown in FIG. 1, or by other techniques whereby significant force may be applied and retained to promote natural healing of the sternum portions 12,14, e.g. mechanical connecting devices such as buckles, etc. See, for example, U.S. Pat. No. 4,813,416. It has been found that such a band has a strength to elongation ratio comparable to stainless

steel. The strength and load carrying capability of the elongated filaments **18** is sufficient to transmit substantial force to the sternum with minimum elongation occurring to the fibers thereby permitting the sternum portions to undergo a natural healing process. Furthermore, in addition to the textile processes of braiding and weaving it should be noted that alternative textile processes may be utilized including knitting techniques, provided that the final product contains a plurality of elongated high strength filaments **18,22** extending along at least the length of the product in the force-carrying direction to maintain the tissue portions together.

The braided product also may be made on a so-called spiroid braider by a method whereby a plurality of filament dispensers are moved in the same direction to different positions around a closed loop. In addition, the braid product may be produced by a conventional braiding process by directing a plurality of yarn dispensers along in equal and opposite undulating paths while directing the filaments or filler fibers toward a common braiding zone. In either process the final braided product will be manufactured to include a plurality of high strength, high molecular weight, high tenacity filaments as disclosed hereinabove, either as a component of the product, e.g. a core, or as the sole material used to construct the product. In addition, the yarn and/or product may be plasma treated depending upon the particular needs or intended application so as to reduce the perceived "slipperiness" of the product as desired.

For example, in any of the braided products disclosed herein the portions of the yarns may be of such high molecular weight, high tenacity filaments while the remaining portions are of absorbable or non-absorbable fibers or filaments. Further, the yarns may also be entirely of such high molecular weight, high tenacity filaments. For such products containing a core, the core may be as noted above, in combination with various types of fibers and/or filaments, absorbable or non-absorbable as described herein.

The final product could be provided with a surgical needle at one or both ends to facilitate insertion of the product into the body tissue whether the body tissue be soft skin tissue or hard bone tissue, or the needles may be utilized to facilitate looping the product into and out of spaces formed between the component members of the body such as the components forming the human sternum. Alternatively, the product could be provided with a needle at each end to facilitate ease of application to the body portions. In either event, the strength and the load carrying filaments **18** and the minimal elongation to strength percentage renders such filaments ideal for incorporation into a final product wherein body portions can be retained together to promote healing. In particular, the formation of a surgical suture repair product utilizing textile processes in combination with bioabsorbable filaments renders the incorporation of high tenacity, high strength, high molecular weight filaments **18** as an ideal combination to form a surgical suture repair product.

The following examples are provided for flat tapes and braids which can be utilized to tie two half portions of a human sternum to promote healing. In the examples which follow, all tapes or braids use Dacron polyester yarn. Braiding of the tapes or braids with Dacron yarns are noted for exemplary purposes only and such yarns may be appropriately substituted with any other suitable bioabsorbable or nonabsorbable yarns, as desired or appropriate for a particular construction. Of course, substitution of different yarns may require variations to the structure as required to accommodate changes in density and/or fiber denier. The fibers may be twisted or air entangled periodically to create a false twist.

EXAMPLE 1

A braided tape of Spectra 1000 high tenacity polyethylene multifilament fibers (60 filaments, 215 denier) was made on a 15 carrier flat tape braider with 7 parallel runners. This structure is shown in FIGS. **4** and **5**. Tests showed the following properties.

Denier =	10,585
Tape Thickness =	0.66 mm
Tape Width =	3.91 mm
Knot pull =	47.5 kg
Straight pull =	66.5 kg
Pick count =	20 crossovers per inch

The tape of this example was made with air entangled rather than twisted yarn. It is contemplated that the yarn could instead be twisted prior to braiding, with all or some of the yarn twisted in either the "s" or "z" directions. Twisted yarn should increase strength and decrease slipperiness of the tape.

EXAMPLE 2

A braided tape having multifilament Spectra 1000 runners (60 filaments, 215 denier) and Dacron fill yarns was made on a 17 carrier braider with 8 parallel runners. This structure is shown in FIGS. **2** and **3**. The Dacron fill yarns were made with three plies of air entangled 100 denier, 54 filament Dacron type 55 yarn. The properties of the tape were measured as follows:

Denier =	7,551
Tape Thickness =	0.34 mm
Tape Width =	3.14 mm
Knot pull =	36.5 kg
Straight pull =	53.6 kg
Elongation at break =	3.4%
Pick count =	26 crossovers per inch

EXAMPLE 3

A braided tape is made with Spectra 1000 runners (60 filaments, 215 denier) and nylon fill yarn. The nylon fill yarn is made from three plies of 100 denier, 34 filament type 385 Dupont bright air entangled nylon yarns. The tape may be made to the desired width, thickness and pick count on any appropriate braider, such as a 15 carrier braider with 7 runners or a 17 carrier braider with 8 runners or a 21 carrier braider with 10 runners.

EXAMPLE 4

A braided tape is made with Spectra 1000 runners (60 filaments, 215 denier) and a bioabsorbable fill yarn such as a yarn made from a copolymer of glycolide and lactide. The bioabsorbable fill yarn may be twisted or air entangled and plied to a total denier of about 300 denier. the tape may be made to the desired width thickness and pick count on any appropriate braider, such as a 15 carrier braider with 7 runners or a 17 carrier braider with 8 runners or a 21 carrier braider with 10 runners.

EXAMPLE 5

A braided tape of plasma treated spectra 1000 high tenacity polyethylene multifilament fibers (60 filaments, 215 denier) was made on a 15 carrier flat tape braider with 7 parallel runners. Tests showed the following properties:

Denier =	5,338
Tape Thickness =	0.40 mm
Tape Width =	3.21 mm
Knot pull =	47.5 kg
Straight pull =	66.5 kg
Elongation at break =	8.6%
Pick count =	25 crossovers per inch

The tape of this example was made with air tangled rather than twisted yarn. It is contemplated that the yarn could instead by twisted prior to braiding, with all or some of the yarn twisted in each of the "s" or "z" directions.

The tape made from plasma treated yarn was perceptibly less slippery than the tape of Example 1, which may be desirable under some circumstances.

EXAMPLE 6

A suture of spiroid braid construction was made on a 15 carrier spiroid braider using Spectra 1000 yarn (60 filament, 215 denier). The braid is shown in FIGS. 6 and 7. The braid had the following properties.

Denier =	3,248
Diameter =	0.832 mm
Knot pull =	32.4 kg
Straight pull =	43.0 kg
Elongation at break =	14%

Spiroid sutures may be made with twisted yarn with a variety of carriers, such as 9, 12, 20 or 25 carriers, as desired to obtain a particular configuration.

EXAMPLE 7

A suture of hollow braid construction having a Spectra 1000 core was made, and is shown in FIGS. 8 and 9. Dacron air entangled bright polyester yarn (40 denier, 8 filament, type 55) was used on the carriers of an 8 carrier braider (4 carriers travelling in the S direction, 4 carriers travelling in the Z direction) to make a sheath surrounding a core of untwisted Spectra 1000 yarn. The properties of the suture were as follows.

Denier =	550
Diameter =	0.20 mm
Knot pull =	3.9 kg
Straight pull =	7.9 kg
Elongation at break =	3.3%

A wide variety of hollow braid constructions are contemplated. Thus, sutures having Spectra 1000 core or components can be made on braiders having 12, 16, 24, 28 or 32 carriers, and numerous yarns can be used to form a sheath surrounding the core, such as bioabsorbable yarn; Dupont Dacron polyester air entangled bright yarn (such as 100 denier, 54 filament type 55 bright yarn or 70 denier, 34 filament type 52 bright yarn); or Dupont air entangled nylon yarn (such as 40 denier, 13 filament type 335 bright yarn or 100 denier 34 filament type 385 bright yarn or 70 denier, 34 filament type 185 bright yarn or 55 denier 17 filament type 865 bright yarn, or 15 denier 7 filament type 180 bright yarn).

The core yarns may be twisted to condense the structure or plied to increase strength and denier. The sheath yarns may also be twisted, if desired.

In the foregoing examples, all physical tests were conducted at 73° F., 50% relative humidity on an Instron Corporation Model 4502 test apparatus. Knot pull tests were performed using a 6 inch gauge length with a 0.5 inch per minute crosshead speed. Straight pulls were made using a 10 inch gauge length with a 10 inch per minute crosshead speed. Yarn or tape grips were used, as appropriate.

While the foregoing description contains many specifics, it will be understood that numerous modifications may be made within the scope of the appended claims. By way of example, a wide variety of yarn substitutions may be made to arrive at various braided tape or hollow and spiroid suture configurations constructed in whole or in part from high tenacity reinforcing fibers. In addition, bioabsorbable and non-bioabsorbable yarns may be substituted as desired to achieve properties and characteristics suitable for a particular situation.

We claim:

1. A method for repairing split portions of body tissue comprising looping a flexible elongated member about the body tissue in a manner to attach the portions in adjacent engaged relation to promote natural healing thereof, said flexible member being formed at least in part of first fibers of ultra-high molecular-weight high tenacity material and at least second fibers which differ from said first fibers and are formed from a non-absorbable material, said first and second fibers being braided to form said elongated member.

2. The method of claim 1 wherein the molecular weight of said fibers is within the range of from about 500,000 to about 5 million.

3. The method of claim 2 wherein said fibers comprise high tenacity extended chain polyethylene fibers.

4. The method of claim 1 wherein said elongate member has an elongation to break below about 15%.

5. The method according to claim 1 wherein said elongate member is of a flat braided construction.

6. The method according to claim 1 wherein said elongate member is of hollow braid construction.

7. The method according to claim 6 wherein said hollow braid contains a core.

8. The method according to claim 1 wherein said elongated member is of spiroid braid construction.

9. The method according to claim 8 wherein said spiroid braid has a substantially circular cross-sectional shape.

10. The method according to claim 1 wherein said elongated member has a straight pull greater than about 35 kg.

11. The method according to claim 1 wherein said second non-absorbable fibers are formed from nylon.

12. The Method according to claim 1 wherein said second non-absorbable fibers are formed from polyester.

* * * * *

Exhibit 21

OSTROLENK, FABER, GERB & SOFFEN, LLP

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Please reply to:
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November 14, 2000

Mr. Don Grafton
Arthrex, Inc.
2885 South Horseshoe Drive
Naples, FL 34104

Re: OFGS Ref: 3/1493-372
U.S. Patent No. 5,318,575 -- Infringement

Dear Don:

In accordance with your request, we conduct a study to determine if Arthrex's proposed PolyBlend suture (a suture with a reinforced jacket formed of polyester braided with Dyneema®, an ultra high strength polyethylene fiber) infringes U.S. Patent No. 5,318,575 issued to Chesterfield, et al., assigned to U.S. Surgical Corporation (the "U.S. Surgical patent").

Briefly, for the reasons set forth below, it is our opinion that Arthrex's PolyBlend suture, and the method of using the suture for surgical suturing, does not infringe the claims of the U.S. Surgical patent.

The U.S. Surgical Patent:

The U.S. Surgical patent has 12 claims, one of which is independent. Independent claim 1 recites a method of repairing split portions of body tissue. A flexible member (i.e., suture) is looped about the body tissue to hold the split portions together. The suture is made by braiding fibers of an ultra high molecular weight high tenacity material and fibers of another, non-absorbable material.

The prosecution history of the U.S. Surgical patent reveals that the applicants submitted claims drawn to a surgical product comprising an elongated member (suture) formed of fibers of a ultra high molecular weight extended chain high tenacity material braided with fibers of

a different material, the "different material" being defined (in some claims) as being non-absorbable. All of these claims were rejected by the Examiner as being unpatentable over U.S. Patent No. 4,819,458 to Kavesh et al. and U.S. Pat. No. 4,792,336 to Hlavacek et al. (copies enclosed). These claims ultimately were canceled by the Applicants. Accordingly, U.S. Surgical relinquished patent coverage of the braided surgical product, and opted to proceed solely with claims directed to the method of using the suture.

As issued, independent method claim 1 recites a method of repairing body tissue by looping the braided surgical product (as described above) "about" split portions of body tissue. Since the braided surgical product was determined to be unpatentable (and the applicant acquiesced in this determination by canceling the product claims), the patentable feature of method claim 1 resides in the step of looping the braided surgical product about the split portions of tissue.

The prosecution history of the U.S. Surgical patent precludes the claimed step of looping the braided surgical product about the split portions of tissue from being construed to include inserting the braided suture product through soft tissue. Significantly, the U.S. Surgical patent discloses the method of looping the suture about tissue (described at col. 4, lines 58 et seq. and shown in Fig. 1) and the method of inserting the surgical product through soft tissue (described at col. 5, lines 41 et seq.) as alternative embodiments. However, the latter embodiment was never claimed. Claims cannot be interpreted in a manner which "recaptures" subject matter which is disclosed in the specification but not claimed. In any event, insertion through soft tissue of a surgical product that contains high strength/modulus polyethylene is not patentable, since it is disclosed in a cited reference, U.S. Patent No. 4,987,665, issued to Dumican et al. (copy enclosed). See col. 6, lines 54-55, col. 13, lines 39-46, and Fig. 3 of Dumican et al. The claims of the U.S. Surgical patent cannot be construed to encompass subject matter in the prior art.

For the foregoing reasons, we conclude that Arthrex's proposed PolyBlend suture and its use in surgical suturing (inserting the suture through soft tissue) does not infringe the claims of the U.S. Surgical patent.

Very truly yours,

OSTROLENK, FABER, GERB & SOFFEN, LLP

Stephen A. Soffen

SAS/PFM:tj
Enclosure

00037679;1

CONFIDENTIAL

ARM 25129

Exhibit 22

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

C.A. NO. 04-12457 PBS

----------x

DePUY-MITEK, INC.,

A Massachusetts Corporation,

Plaintiff,

vs.

ARTHREX, INC.,

A Delaware Corporation,

Defendants.

----------x

DEPOSITION OF DR. MATTHEW HERMES

Philadelphia, Pennsylvania

June 27, 2006

Reported by:

CONSTANCE S. KENT, CSR, RPR

JOB NO.: 350

Q. Claim 12, is there any mention of a core?

A. No.

Q. Would you agree that in claim one, the -- would include a product that's -- where the two fibers are braided together and there's no core?

MR. BONELLA: Hold on a second. I'm going to object to the form.

THE WITNESS: Would I agree that -- your question is, if I understand it, would I agree that in claim one the two fibers are braided together without a core; is that what you're saying?

BY MR. SABER:

Q. Would that include two fibers braided together without a core?

MR. BONELLA: I object to the form.

THE WITNESS: Yes, it could include two fibers braided together without a core.

BY MR. SABER:

Q. And would the same thing be true for claim 11, that it would include two fibers braided together without a core?

MR. BONELLA: Object to the form.

THE WITNESS: Repeat the question again, Mr. Saber.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

DePuy Mitek, Inc. a Massachusetts Corporation Plaintiff, v. Arthrex, Inc., *et al.* a Delaware Corporation Defendant.	)	Civil Action No. 04-12457 PBS

DECLARATION OF DR. DEBI PRASAD MUKHERJEE

1. My name is Dr. Debi Prasad Mukherjee. I am an Associate Professor and the Coordinator of Bioengineering in the Department of Orthopaedic Surgery at the Louisiana State University Health Sciences Center, in Shreveport, Louisiana. My CV is attached as Ex. A.

2. I am the same Dr. Debi Prasad Mukherjee who prepared the "Expert Report of Dr. Debi Prasad Mukherjee Concerning Invalidity of U.S. Patent No. 5,314,446" dated March 3, 2006, the "Responsive Expert Report of Dr. Debi Prasad Mukherjee Concerning Non-Infringement of U.S. Patent No. 5,314,446 and Other Matters" dated March 24, 2006, and the "Rebuttal Expert Report of Dr. Debi Prasad Mukherjee" dated April 13, 2006.

3. I have been asked to provide my opinion regarding the relative stiffness and the relative tensile strength of ultra high molecular weight polyethylene (UHMWPE) fiber and general purpose polyethylene fiber.

4. It is my opinion that UHMWPE fiber is greater than approximately 100 times more stiff than the general purpose polyethylene fiber to which it is being compared. That is, the general

purpose polyethylene fiber is greater than approximately 100 times more pliable than UHMWPE fiber.

5. My opinion regarding the relative stiffness of UHMWPE fiber and general purpose polyethylene fiber is based on the fact that UHMWPE fiber has a tensile modulus on the order of 117GPa (Giga-Pascals) (Ex. B at 5-26), whereas general purpose polyethylene fiber has a tensile modulus on the order of 0.849GPa. Ex. C at Figure 12 (HMW HDPE). The higher a fiber's tensile modulus, the more stiff the fiber. Accordingly, the general purpose polyethylene would be considered a pliable substance when used with suture and UHMWPE would be considered a stiff material when applied to suture.

6. It is also my opinion that UHMWPE fiber is greater than approximately 60 times stronger than the general purpose polyethylene fiber. That is, the general purpose polyethylene fiber is greater than approximately 60 times weaker than UHMWPE fiber.

7. My opinion regarding the relative strength of UHMWPE fiber and the general purpose polyethylene fiber is based on the fact that UHMWPE fiber has a tensile strength on the order of 2590MPa (Mega-Pascals) (Ex. B at 5-26), whereas the general purpose polyethylene fiber has a tensile strength on the order of 40MPa. Ex. C at Figure 11 (HMW HDPE).

8. It is my opinion that UHMWPE is one of the strongest synthetic fibers ever created. Ex. B at 5-26.

9. It is also my opinion that general purpose polyethylene has been used in industry for decades and has established itself as a general purpose commodity polymer.

10. Since its introduction in fiber form in the 1980s, UHMWPE, has been considered a specialized high performance product. Ex. B at 5-26.

11. The key structural characteristics – molecular weight and molecular structure – of UHMWPE are very different than that of general purpose PE. Ex. D at 4.

12. UHMWPE has a molecular weight of up to approximately 6 million, whereas general purpose PE has a molecular weight of up to approximately 200,000. Ex. D at 4.

13. UHMWPE also exhibits a much higher degree of crystalline orientation as compared with general purpose PE. These differences in molecular structure are the basis for UHMWPE's superior strength characteristics. Ex. D at 4, 6.

14. It is well known in the surgical suture art that a suture must be sterilized before it can be used in any surgical application.

15. FDA Publication "510K Sterility Review Guidance K90-1; Guidance for Industry and FDA" governs the sterilization of medical devices, including surgical suture. Ex. E.

16. It is my opinion that a person of ordinary skill in the surgical suture art would understand that the suture disclosed in U.S. Patent No. 5,318,575 must be sterilized before it can be used in a surgical application.

I hereby declare under penalty of perjury that the foregoing is true and correct.

Executed on: Sept 15, 2006

Debi Prasad Mukherjee

Dr. Debi Prasad Mukherjee

EXHIBIT A

CURRICULUM VITAE

Name

Debi Prasad Mukherjee, Sc.D.

Title

Associate Professor and Coordinator of Bioengineering
Department of Orthopaedic Surgery
Louisiana State University Health Sciences Center

Address

1501 Kings Highway, P.O. Box 33932
Shreveport, Louisiana 71130

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Date of Birth

October 26, 1939

Family

Wife: Bandana
Sons: Avik
Shomik

Education

1961 B.Ch.E. (Hons), Chemical Engineering, Jadavpur University
1965 S.M., Biochemical Engineering, M.I.T.
1965 S.M., Chemical Engineering, M.I.T.
1967 Ch.E., Chemical Engineering, M.I.T.
1969 Sc.D., Chemical Engineering, M.I.T.
1980 M.B.A., Business Administration, University of Connecticut

Employment History

1992-Present Associate Professor and Coordinator of Bioengineering
Louisiana State University Health Sciences Center, Shreveport, Louisiana

1991-1992 Development Scientist
Union Carbide, Bound Brook, New Jersey

1987 - 1990 Research Program Manager
Dow Corning Wright, Arlington, Tennessee

1974 - 1987 Technical Specialist, Biomaterials
Group Leader, Extrusion & Materials Development
Senior Research Engineer

Davis & Geck, American Cyanamid Company, Danbury, Connecticut

1969 - 1974 Senior Research Engineer
The Goodyear Tire & Rubber Company, Akron, Ohio

Academic Appointment

1989 - 1993 Adjunct Associate Professor, Biomedical Engineering
Memphis State University, Memphis, Tennessee

1992 - Present Adjunct Associate Professor, Biomedical Engineering
Louisiana Tech, Ruston, LA.

Thesis Supervised

1. M.S. Thesis (1992) by J. D. Ray Jr. "A Comparison of Fatigue Behavior for APC-2/AS4 and Comningled PEEK/AS-4 Composite", Dept. of Biomedical Engineering, Memphis State University, Memphis, TN.

2. M.S. Thesis (1992) by R. R. Shults, "A Characterization Study of Hydroxylapatite Coatings on Titanium Alloy Implant Material Before and After Fatigue", Dept. of Biomedical Engineering, Memphis State University, Memphis, TN.

3. M.S. Thesis (1993) by H. A. Mansour, "Bone/Prosthesis Relative Rigidity as an Important Parameter in the Isoelasticity of Total Hip Arthroplasty of the Human Proximal Femur", Department of Biomedical Engineering, Memphis State University, Memphis, TN.

4. M.S. Thesis (1994) by P. R. Menon, "Composites of Hydroxylapatite with Water Soluble or Biodegradable Polymers as a Synthetic Bone Graft Material", Louisiana Tech University, Ruston, LA.

5. M.S. Thesis (1996), by S. Ashroff, "Effect of Crystallinity of Hydroxyapatite Coating on Titanium Implants After Cyclic Fatigue Loading", Louisiana Tech University, Ruston, LA.

6. M.S. Thesis (1996), by N.R. Dorairaj, "Effects of Cyclic Fatigue Loading on the Stability of Hydroxyapatite Coated Titanium Dental Implants in the Presence of the Periodontal Pathogens", Louisiana Tech University, Ruston, LA.

7. M.S. Thesis (1999) by J.R.Hunter, "The measurement of Stress shielding and Relative Rigidity Mismatch within the femur prosthesis union of Total Hip Replacement" Louisiana Tech University, Ruston, LA.

8. Ph.D. Thesis (2001) by Kelly Crittenden, "Evaluation of 135- and 150-degree

Sliding hip screws". Louisiana Tech University, Ruston, LA.

Honors and Awards

1. MNC Memorial Medal for securing the highest grade in the Sophomore Class of the Chemical Engineering Department, 1958.

2. E.F Berkman, RN Kruse, DP Mukherjee, KK Sadasivan, and JA Albright: A study of burst fracture in a canine model, Louisiana Orthopaedic Association, Harry Morris Award, 1993.

3. JW Sikes, BR Smith, DP Mukherjee, and KA Coward: "Comparison of Fixation of Locking Head and Conventional Screws in Fracture and Reconstruction Models." Winner of American College of Oral and Maxillofacial Surgeons Resident Research Award 18th Annual Meeting, San Diego, CA.,1997.

4. JW Sikes, BR Smith, and DP Mukherjee: "Effect of Bony Buttressing in the Atrophic Edentulous Mandible: An In Vitro Study." Winner of ITI Straumann Research Award, AAOMS 80th Annual Meeting, September 1998.

5. R Bhati, DP Mukherjee, KJ McCarthy, S Rogers, and DF Smith: "The Effect of Fibronectin Coating on the growth of Chondrocytes into a Biodegradable Scaffold." National Student Research Forum- The University of Texas Medical Branch of Galveston Texas, Department of Orthopaedic and Rehabilitation Award, 2000.

Editorial Board

Journal of Long Term Effect of Medical Implants
(Member of Editorial Advisory Board) 1998- Present

Journal of Biomedical Materials Research (Applied Biomaterials)
(Member of Editorial Board) 1998-2002.

Conferences Organized

Akron Polymer Lecture Group

Secretary, 1972
Program Chairman, 1973

14th Southern Biomedical Engineering Conference

Chairman
April 7-9, 1995, Shreveport, LA

Technical Sessions Chaired

Biomaterials:

11th Southern Biomedical Engineering, Memphis, TN (1992), Session Chairman

Determination of Bone Properties:

12th Southern Biomedical Engineering, New Orleans, LA (1993), Session Chairman

Biomechanics and Biomedical Engineering Symposium

Orthopaedics Biomechanics I: 31st Annual Technical Meeting of the Society of Engineering Science, Texas A&M (1994) Session Co-Chairman

Orthopaedic Biomechanics

13th Southern Biomedical Engineering, Washington, D.C. (1994)- Session Chairman

Dental Materials: natural dentition polymers and composites

Sixth World Biomaterials Congress, Hawaii (2000) Session Co-moderator

Polymers in Orthopaedics Symposium (American Chemical Society) August 2002

Chaired the session

Public/Community Service Activities

NIH Proposal Evaluations and Site Visits:

1. Reviewed the contracts on the biocrodible drug-delivery systems and was invited to a site visit to SRI on May 5-7, 1987, by the Contraceptive Development Branch, Center for Population Research, National Institutes of Health and Human Development - NIH contract, Dr. Dinesh Sharma.
2. Reviewed a number of proposal on drug-delivery systems and was invited for a working group in Bethesda, Maryland, on April 27, 1990, NIH contacts, Dr. H. Khan and Dr. D. Sharma.

3. Reviewed proposals on "Development and Testing of New Spermicides for National Institute of Child Health and Development", Bethesda, MD. June 16-17, 1992, NIH contact, Dr. S. Strenfert.
4. Special Study Section - Small Business Innovation Research (SBIR) Program, Rockville, MD, July 6-8, 1994, NIH contact, Dr. N. Vydelingum.
5. Task Group Chair, Scaffold Biomaterials Section, American Society of Testing and Materials (ASTM) 1998- 2001

Institute Activities

1992 - Present	Mentor ;Minority High School Student Research Apprentice Program
1992 - Present	Mentor: Summer Medical Student Research Program
1994 - 1995	Member of the Medical Communication Committee
1998-at present	Mentor: Science Medicine Academic Research Training Program
2001- Present	Flag Group Leader: Module III-New curriculum of instructions to Freshman/Sophomore Medical Students
2003-Present	Member of Institutional Review Board

Invited Lecturer:

Baylor College of Medicine, Department of Orthopaedic Surgery, -Grand Round – Plaster of Paris as a vehicle for delivery of tobramycin to treat Osteomyelitis, March, 13, 1994

Biomaterials Seminar in Atlanta: Technomic Publishing Co. Inc.
Tissue Engineering Applications of Bioabsorbable Polymers, November 16, 1999

Baylor College of Medicine, Department of Orthopaedic Surgery, - Grand Round Baylor University Medical center, Houston, TX, Meniscal Repair, May 7, 2003

Society Membership

Orthopaedic Research Society
Society for Biomaterials
American Association of Advancement of Science

Research Support and Meeting Grants

1. American Heart Association, Akron Chapter, December 10, 1973, for the project, The Relationship of Dynamic Mechanical Properties of Arteriosclerotic Tissue to the Deposit of Cholesterol and Its Ester, jointly with Dr. Thomas Pynadath of Kent State University, Kent, Ohio 44242, $8030.00

2. School of Dentistry, LSU Medical Center, and New Orleans. "Biomechanical In Vitro testing of the stability of HA coating etc.", jointly with Dr. J. Wittenberg, Department of Surgery, Division of Oral and Maxillofacial Surgery LSUMC-S, 1993, $7500.00.

3. ExacTech Inc., Gainesville, FL. "Experimental testing of components comprising the ExacTech 913 Knee System." 1993, $150.00

4. Whitaker Foundation: Fourteenth Southern Biomedical Engineering Conference, 1994, $6,000.00.

5. Smith & Nephew Richards: Fourteenth Southern Biomedical Engineering Conference, 1994, $1,000.00.

6. Sofamor Danek Medical: Fourteenth Southern Biomedical Engineering Conference, 1994, $300.00.

7. Dean - LSU School of Medicine-Shreveport: Fourteenth Southern Biomedical Engineering Conference, 1994, $4,500.00.

8. Center of Excellence for Arthritis & Rheumatology: 1992-1994, $37,070.00

9. Ortho-Care, Inc: 1994, $550.00.

10. Chitogenics, Inc.: Nov. 1995-May 1996, Evaluation of the carboxymethyl chitosan (NOCC) and hydroxyapatite composite paste for repairing bone defects in a rat model. Feasibility of using NOCC to complex with the hyaluronic acid to reduce the drop of viscosity of synovial fluids of the rheumatoid patients. $10,000.00.

11. Intramural Grant: January 1, 1997 - December 31, 1997. Tissue Engineering - Development of Scaffolds seeded with Different Cell types on a biodegradable matrix. $5,000.00.

12. Wright Medical Technology: June 15, 1997 - Feb. 1999. Measurement of Creep Properties of Bone Cement. $15,000.00

13. Louisiana Board of Regents: Travel Grant for Emerging Faculty. $500.00.

14. Celanese Acetate: November, 15, 1998- November 15, 1999. Feasibility study of modification of cellulose acetate filters (CAF) by gamma and electron beam radiations. $7,060.00.

15. Board of Regents Support fund, June 2000-June 2001 with matching grant from LSUHSC: Replacement of Biaxial Testing machine (Instron Model 1321) by a new digital biaxial machine (Model 8874): **$117,732.**

16. Clinical and Industrial technology Company, July 2000- July 2001: A New Vibration Mixer for Bone Cement: **$14,000.**

17. Department of Obstetrics & Gynecology , 2002-2003: "Biomechanical Studies on several Sutures". **$3420.**

18. W.L.Gore and Associates, Biodegradable Scaffold for Tissue Engineering , Jan -May 2004, **$5000.**

PUBLICATIONS

Research Thesis

D. P. Mukherjee, The Viscoelastic Properties of Elastin, Sc.D. Thesis in the Department of Chemical Engineering, M.I.T., January 13 (1969).

Papers and Abstracts of Presentations

1. DP Mukherjee and A.S. Hoffman: The Viscoelastic Properties of Elastin. Presented at the Third Biophysics Congress, August (1969).

2. A.S. Hoffman and DP Mukherjee: long-range Interactions of Cationic Sites in Elastin. Presented at the Conference on Engineering in Medicine and Biology, October 31(1971).

3. DP Mukherjee and C. Goldstein: The Mechanical and Optical Properties of Alternating and Random Copolymers of Acrylonitrile and Butadiene at the Same Acrylonitrile Content. Polymer Preprints, Vol. 14, No. 1, 36-39, (1973).

4. DP Mukherjee and C Goldstein: The Mechanical and Optical Properties of an Alternating and Emulsion NBR. Rubber Chemistry and Technology, 46, 1264-1273, (1973).

5. DP Mukherjee, AS Hoffman, and C Franzblau: The Physical Properties and Molecular Structure of Ligamentum Nuchae Elastin. Biopolymer, Vol. 13, 2447-2459, (1974).

6. DP Mukherjee and MC Morris: Rheological Properties of Synthetic Poly (isoprene) and Natural Rubber. Presented at the Annual Meeting of the Society of Rheology, Amherst, Massachusetts, October, (1974).

7. DP Mukherjee: Simultaneous Stress-Strain and Stress-Birefringence Studies on Natural Rubber, Isomerized Natural Rubber and Synthetic Poly (isoprene). Rubber Chemistry and Technology, Vol..47, No. 5,1234-1240, (1974).

8. DP Mukherjee, H.M. Kagan, R.E. Jordan, and C. Franzblau: Effect of Hydrophobic Elastin Ligands on the Stress-Strain Properties of Elastin Fibers. Connective Tissue Research, 4, No. 3, 177-179, (1976).

9. DP Mukherjee and TI Pynadath: The Relationship of Dynamic Mechanical Properties of Arteriosclerotic Tissue of Cholesterol and Cholesterol Ester Levels of Serum and Aortic Tissues During Early Stages of Development of Atherosclerosis. Atherosclerosis, 26, 311-318, (1977).

10. DP Mukherjee: A Study of Flow Properties of Rubbers Using Rheometrics Mechanical Spectrometer. Polymer Engineering and Science, November 17, No. 1, 788-792, (1977).

11. AR Katz, D.P. Mukherjee, AL Kaganov, and S Gordon: A New Synthetic Monofilament Absorbable Suture Made from Polytrimethylene Carbonate. Surgery. Gynecology and Obstetrics, September, Vol. 161, 213-222, (1985).

12. DP Mukherjee and C Sandock: Effect of Gamma Irradiation on the Properties of the Glycolide/Trimethylene Carbonate Copolymer Maxon® Suture. The Third World Biomaterials Congress, April 21-25, 1988, Kyoto, Japan.

13. DP Mukherjee and JG Brooks, Jr.: Mechanical and Non-Destructive Evaluations of a Carbon/Carbon Composite Material. 37th Annual Meeting, Orthopedic Research Society, March 4-7,1991, Anaheim, California, 498.

14. DP Mukherjee and S Saha: Isoelasticity: A Design Consideration of Total Hip Replacement. Digest of Papers 11th Southern Biomedical Engineering, October 2-4, 1992, Memphis, TN, pp 25-27.

15. S Saha and DP Mukherjee: Use of Composite Materials for Total Hip Arthroplasty. Digest of Papers 11th Southern Biomedical Engineering, October 2-4, 1992, Memphis, TN, pp 93-96.

16. JD Ray and DP Mukherjee: A Comparison of Fatigue Properties of Carbon Fiber/PEEK Composites. Digest of Papers 11th Southern Biomedical Engineering, October 2-4, 1992, Memphis, TN, pp 142-144.

17. RR Shults, DP Mukherjee, and JD Ray: A Study of Hydroxylapatite Coated Titanium Alloy Material After Fatigue. Digest of Papers 11th Southern Biomedical Engineering, October 2-4, 1992, Memphis, TN, pp 159-161.

18. JJ Lorio, RN Kruse, DP Mukherjee, and JA Albright: Compressive Strength and Quantitative CT Measurements of Cancellous Bone Sample. 34th National Student Research Forum. The University of Texas Medical Branch, Galveston, Texas, April 15-17, 1993.

19. JJ Lorio, RN Kruse, DP Mukherjee, and JA Albright: Quantitative Computer Tomography (QCT) and Mechanical Properties of Cancellous Bone. Proceedings of the Twelfth Southern Biomedical Engineering Conference, New Orleans, LA, April 2-4, 1993, pp 242-244.

20. RN Kruse, DP Mukherjee, and JA Albright: A Method of Quantitative Analysis of Computed Tomography (QCT) Scan of Bone Samples Using a Sun Workstation. Proceedings of the Twelfth Southern Biomedical Engineering Conference, New Orleans, LA, April 2-4, 1993, pp 37-39.

21. DP Mukherjee, T Sweo, and JA Albright: A Comparative Study of Femoral Neck Fracture Fixation by a Compression Screw or Knowles Pins. First Joint ASCE/ASME

Summer Meeting and SES 30th Annual Meeting: Biomaterials and Biomechanics Symposium, Charlottesville, VA, June 6-9, 1993, pp 61.

22. DP Mukherjee and S. Saha: The Application of New Composite Materials for Total Joint Arthroplasty. Journal of Long Term Effects of Medical Implants, 3 (2): 131-141 (1993).

23. AD McBride, DP Mukherjee, RN Kruse, and JA Albright: Anterior Screw Fixation of Type II Odontoid Fractures: A Biomechanical Study. Poster presentation 21st Cervical Spine Research Society Meeting, New York, December 1-4, 1993.

24. EF Berkman, RN Kruse, DP Mukherjee, KK Sadasivan, and JA Albright: Relationship Between Bone Mineral Density and Burst Fracture Load: A Biomechanical Study. Transactions of Orthopaedic Research Society, 19(2): 530, 1994.

25. DP Mukherjee, JM Wittenberg, SH Rogers, RN Kruse, and JA Albright: Surface Changes of Hydroxyapatite Coated Dental Implants After Cyclic Loading. Transactions 20th Annual Meeting of the Society for Biomaterials, 17:7, 1994.

26. JD Ray Jr., DP Mukherjee, and JD Ray: The Fatigue Properties of Carbon Fiber/PEEK Composites: Transactions 20th Annual Meeting of the Society for Biomaterial, 17:161, 1994.

27. RR Shults, DP Mukherjee, and JD Ray: A Study of Fatigue Properties of Hydroxyapatite Coated Titanium Alloy Implant Materials. Transactions 20th Annual Meeting for the Society for Biomaterials, 17:333, 1994.

28. DP Mukherjee, S Rogers, S Foster, KK Sadasivan, and JA Albright: A Histological Study of Polyethylene Particles in a Rabbit Model. Transactions of the 20th Annual Meeting of the Society for Biomaterials, 17:392, 1994.

29. EF Berkman, RN Kruse, DP Mukherjee, KK Sadasivan, and JA Albright: A Comparative Biomechanical Evaluation of the Thoracolumbar Burst Fracture in Human and Canine Specimens. Orthopaedic Transactions, J Bone Joint Surg., 18(2): 517, 1994.

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EXHIBIT B

(1)

Engineers' Guide to Composite Materials

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This book is a collective effort involving a large number of technical specialists. It brings together a wealth of information from world-wide sources to help scientists, engineers, and technicians solve current and long-range problems.

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Mechanical Properties of Aramid, Polyamide, Polyester, and Nylon Fibers

Fiber	Density Mg/m³	Density lb/in.³	Tensile strength MPa	Tensile strength ksi	Tensile modulus GPa	Tensile modulus 10^6 psi	Ultimate elongation, %
Aramid-Kevlar 29	1.44	0.052	3620	525	83	12	4.4
Aramid-Kevlar 49	1.44	0.052	3620	525	124	18	2.9
Polyamide	1.13	0.041	830	120	2.8	0.4	...
Polyester-Dacron Type 68	1.38	0.050	1120	162	4.1	0.6	14.5
Nylon–Du Pont 728*	1.13	0.041	990	143	5.5	0.8	18.3
Spectra-900	0.97	0.035	2590	375	117	17	...

*Unimpregnated twisted yarn test–ASTM D2250.

Effect of Tension-Tension Fatigue on Aramid (Kevlar 29) Fibers (Du Pont Co.)

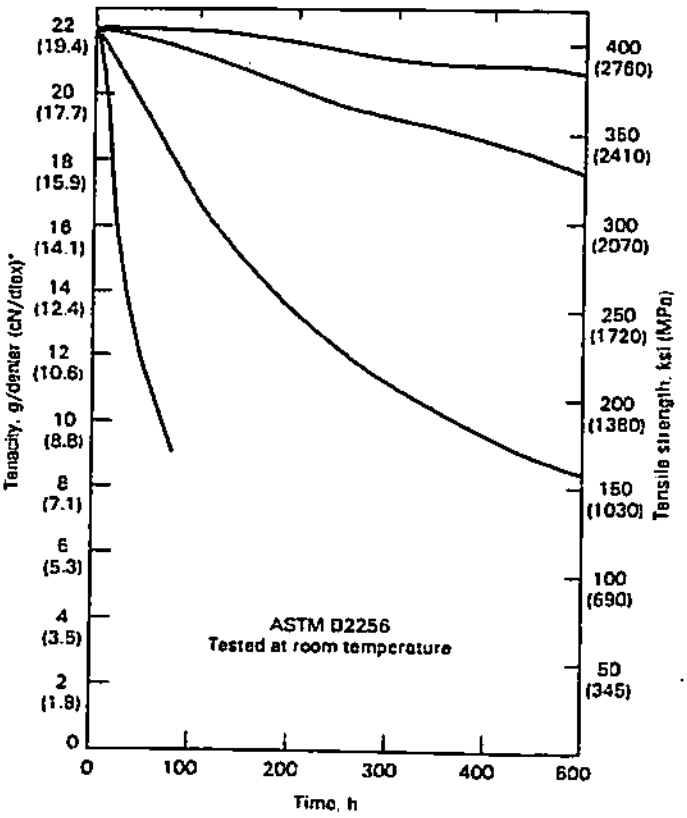
Cycled between (% of ultimate tensile strength) High	Low	No. of cycles	Break load after cycling N	Break load after cycling lb	Decrease in tensile strength due to fatigue
Control		...	552	124	...
74	45	1000	578	130	None
52	29	1000	610	137	None
31	8	1000	587	132	None
10	0	13×10^6	525	118	5%

1500 denier [1670 dtex] 2-ply yarn of Kevlar 29 was tested using air-actuated 4-D cord clamps on an Instron test machine, at 254 mm (10 in.) original gage length, 10% per minute elongation, 55% R.H., and 22 °C (72 °F).

Coating Materials Used Successfully With Kevlar 29 Aramid Fiber (Du Pont)

Coating	Typical end uses
Neoprene synthetic rubber	Inflatable boats
Hypalon synthetic rubber	Pond liners, tarpaulins
Nitrile rubber	Pressure diaphragms
Nordel hydrocarbon rubber	Heat-resistant conveyor belts
Buna-N	Hoses
Urethane polymers	Inflatable structures
Silicon and fluorosilicon	Belting
Polyvinyl chloride	Air-supported structures
Teflon [TFE, FEP] fluorocarbon resin	Nonstick belts
Polyvinyl alcohol	Specialty uses
Laminations: Tedlar polyvinyl fluoride / Mylar polyester	Lighter-than-air craft

Effect of Temperature on Tensile Strength of Aramid (Kevlar 29) Fiber (Du Pont Co.)



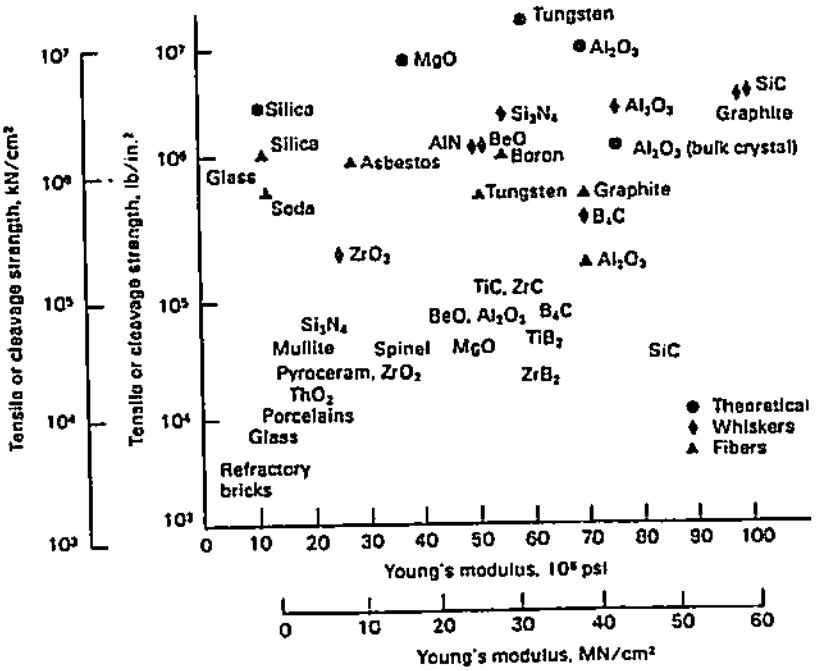
*Conversion factor: $\frac{\text{lb}}{\text{in}^2} = \left(\frac{\text{g}}{\text{denier}}\right) \times \text{density}\left(\frac{\text{g}}{\text{cm}^3}\right) \times 12\,800$

Chemical Resistance of Kevlar (Ref 34)

Chemical	Concentration, %	Temperature °C	Temperature °F	Time, h	Strength loss, % Kevlar 29	Strength loss, % Kevlar 49
Hydrochloric acid	37	21	70	100	72	63
Hydrochloric acid	37	21	70	1000	88	81
Hydrofluoric acid	10	21	70	100	10	6
Nitric acid	1	21	70	100	16	5
Nitric acid	10	21	70	100	79	77
Sulfuric acid	10	21	70	100	9	12
Sulfuric acid	10	21	70	1000	59	31
Sodium hydroxide	10	21	70	1000	74	53
Ammonium hydroxide	28	21	70	1000	9	7
Acetone	100	21	70	1000	3	1

(continued)

Strength Vs. Modulus for Tungsten and Various Ceramics in Bulk, Fiber, and Whisker Forms (Ref 8, p 359)

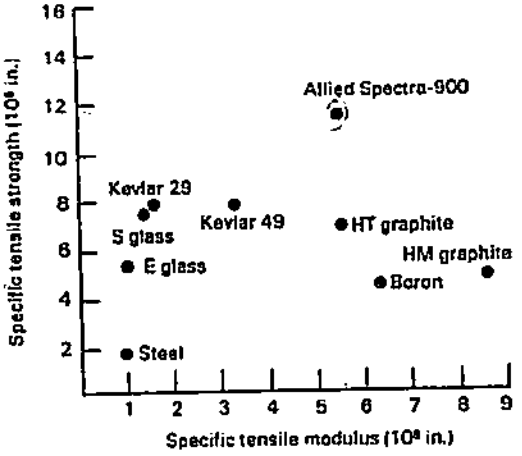


Comparative Mechanical Properties of Kevlar, Glass, and Graphite Fibers (Du Pont Co.)

Property	Kevlar 29	E glass	Graphite
Tensile strength*:			
MPa	3620	3415	2760
ksi	525	350	400
Tensile modulus*:			
GPa	82.7	68.9	220
10^6 psi	12	10	32
Density:			
g/cm³	1.44	2.52	1.74
lb/in.³	0.052	0.091	0.063
Brittleness	Tough	Brittle	Brittle
Abrasiveness	No	Yes	Yes

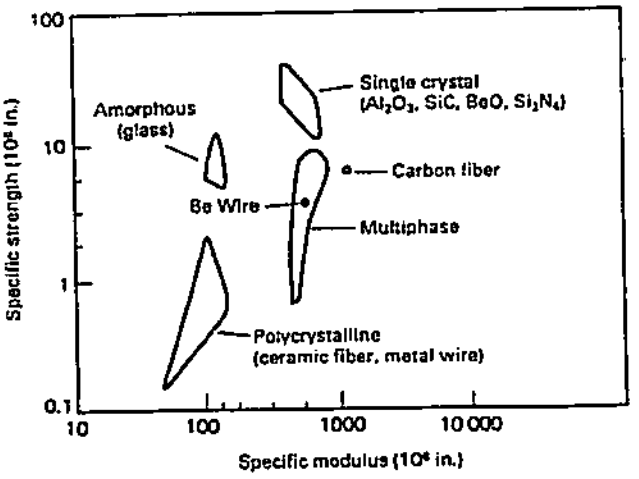
*Resin-impregnated strand test.

Specific Strength Vs. Specific Modulus for Reinforcing Fibers (Allied Fibers)



Room-Temperature Specific Strength and Specific Stiffness of Several Fibers (Ref 11, p 25)

Specific values in this figure were determined by dividing strength or modulus by density, expressed in lb/in.³ or kg/M³.



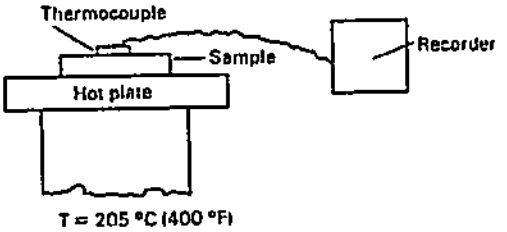
Characteristics of Carbon-Boron Alloy Fiber Groups (Ref 73)

Characteristic	Group A	Group B	Group C	Group D
Carbon interlayer	No	No	Yes	Yes
Number of CVD reaction chambers	4	3	3	3
Boron content*, wt %	43–46	35–39	46–48	48–51

*Unpublished research, D. L. McDanels, NASA Lewis Research Center.

Thermal Conductivity of Kevlar Felts and Fabrics Vs. Other Materials (Du Pont Co.)

Fabric	Weight g/m²	Weight oz/yd²	Thickness mm	Thickness mils	Lag time, s	Thermal conductivity, cal/cm²·s·°C	Temperature rise in 25 s °C	Temperature rise in 25 s °F
Kevlar 29 (1 ply)	333	9.8	0.76	30	0	0.324	60	108
Kevlar 29 (3 ply)	998	29.4	2.16	85	3	0.162	30	54
Kevlar 29 (felt)	917	27.0	2.67	105	1.5	0.084	16	28
Fiberglass (1 ply)	285	8.4	0.30	12	0	0.600	111	200
Fiberglass (8 ply)	2282	67.2	2.16	85	5.1	0.105	19	35
Asbestos	1386	40.8	2.29	90	2.5	0.168	31	55



Schematic of Test Apparatus for Determining Lag Time

Lag time is time between placing sample in contact with hot plate and any perceptible recorder readout.

Some Typical Fabric Dimensions (Hexcel-Trevarno)

Construction	Weave	Thickness, mils	Width, in.	Weight, oz/yd²
Graphite				
12.5 × 12.5	Plain	7.2	42	5.7
24.0 × 24.0	Satin	13.5	42	10.0
10.5 × 10.5	Plain	6.0	42	5.5
10.0 × 24.0	Plain	6.1	38	4.7
Kevlar				
34 × 34	Plain	4.5	38	1.8
50 × 50	Satin	11	38	5.0
22 × 22	Plain	4.5	38	2.2
17 × 17	Plain	10	38, 50	5.0
17 × 17	Crowfoot	10	38, 50	5.0
13 × 13	Plain	10	50	5.0
16 × 16	Satin	13	50	9.0
28 × 28	Basket	20	50	10.5
26 × 22	Basket	20	44, 50, 60	13.5
17 × 30	Plain	7	38	3.1
S Glass				
24 × 22	Plain	5.5	38	3.7
18 × 18	Plain	9	38	5.8
48 × 30	Crowfoot	9	30	8.8
57 × 30	Crowfoot	5.5	38	5.4
57 × 54	Satin	8.5	38	8.9
Ceramic				
48 × 47	Satin	9.0	38	7.5

Comparative Textile Fiber Properties (Ref 90)

	Spectra 900	Spectra 1000	Aramid LM	Aramid HM	Carbon HT	Carbon HM
Denier/Number of filaments	1200/118	650/120	1500/1000	1500/1000	1730/3000	1630/3000
Tenacity, g/d	30	35	22	22	20	14
Elongation, %	3.5	2.7	3.6	2.8	1.2	0.6
Tensile modulus, g/d	1400	2000	488	976	1500	2400
Shrinkage at boil, %	<1	<1				
Specific gravity	0.97	0.97	1.44	1.44	1.73	1.81
Melting point, °C	147	147				
Filament size, μm	38	27	12	12	7.0	6.5

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EXHIBIT C

JOURNAL OF APPLIED POLYMER SCIENCE VOL. 18, PP. 2539-2568 (1974)

Interaction of Melt Spinning and Drawing Variables on the Crystalline Morphology and Mechanical Properties of High-Density and Low-Density Polyethylene Fiber

JAMES L. WHITE, KHUSHAL C. DHAROD, and EDWARD S. CLARK, *Department of Chemical and Metallurgical Engineering, The University of Tennessee, Knoxville, Tennessee 37916*

Synopsis

An experimental study of the spinnability and the variation in crystallinity and orientation in high-density and low-density polyethylene fibers with melt spinning and drawing conditions has been carried out. Three polymers (two high-density and one low-density) and eicosane ($C_{20}H_{42}$) were studied. The maximum spinnability was in the lower molecular weight high-density polyethylene. Hermans-Stein a, b, and c crystallographic axis orientation factors were computed from wide-angle x-ray scattering patterns. In the spun fiber, small take-up velocities cause the b axis to become perpendicular to the fiber axis in each fiber. The c axis increasingly orients itself parallel to the fiber axis as take-up velocity increases. The a axis orientation is different for each polymer. The results are interpreted in terms of modern theories of crystalline morphology, specifically the development of row structures. In the drawing experiments, the two high-density polyethylenes necked. A phenomenological theory of necking is discussed. The a, b, and c axis orientation factors were determined for different stages of drawing. In the necked regions and in completely drawn fibers, the c axis was parallel to the fiber axis and the a and b axes are perpendicular to the fiber axis. The tangent Young's modulus and tensile strength of the spun fibers increased with take-up velocity and in the drawn fibers were an order of magnitude higher than in the spun fiber. The mechanical properties of spun fiber may be correlated with the c axis (Hermans) orientation factor. The drawn fiber shows significant variations in Young's modulus and tensile strength at constant unit cell orientation.

INTRODUCTION

The production of fibers from polymer melts generally involves two steps. First, melt is extruded producing a vertical descending thread which is cooled in transit and taken up on a godet in solidified form. This process is known as *melt spinning*. The spun fiber is then subjected to a second operation in which it is unwound from a slow roll, stretched (drawn) under controlled temperature conditions, and taken up on a fast roll. This second process is known as *drawing*. A wide range of spinning and drawing variables is available to the fiber manufacturer. The choice is one not to be taken lightly or completely on the basis of economic considerations for the

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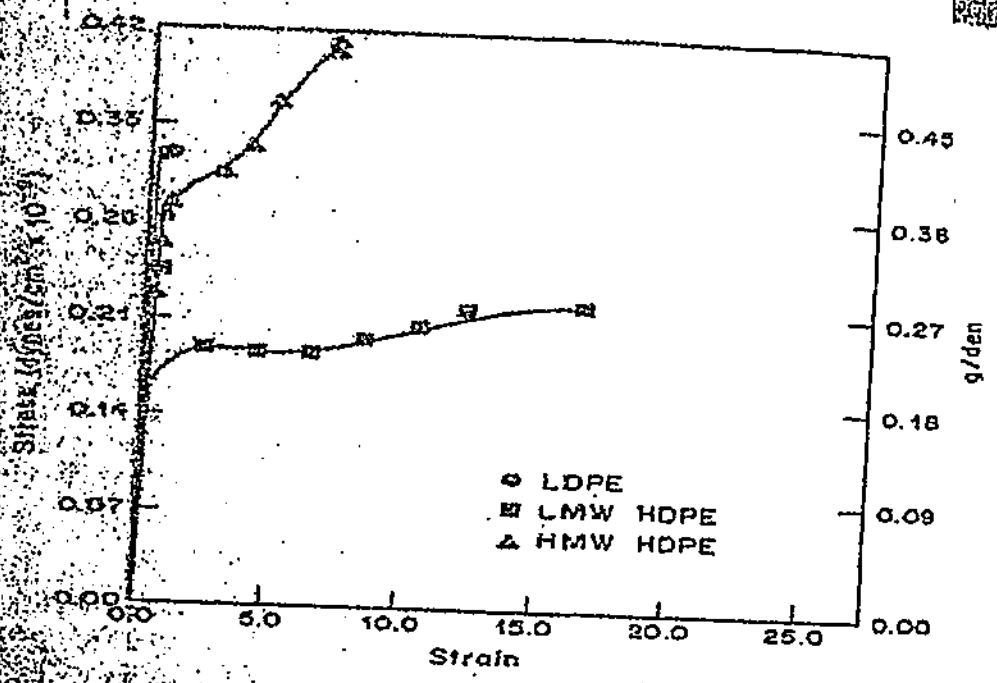

Fig. 11. Stress–strain curves for three different polyethylene fibers spun under the same conditions.

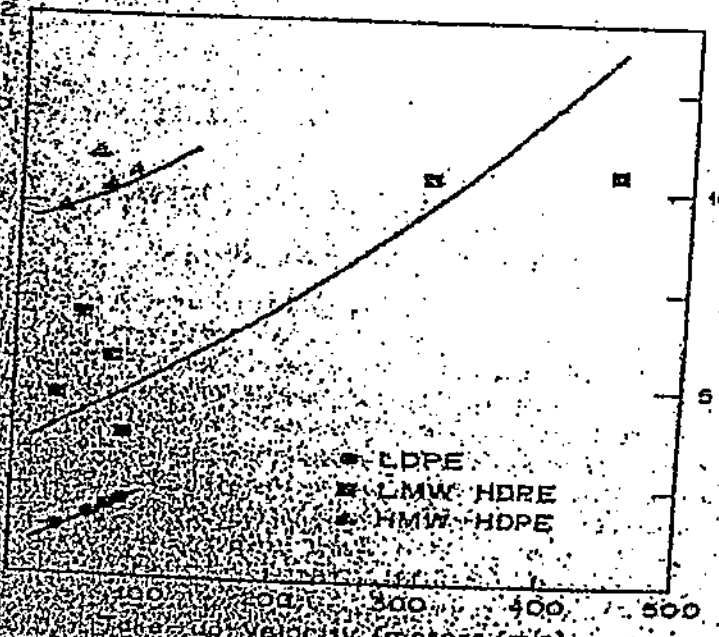

Fig. 12. Stress at break for three polyethylene fibers as a function of take-up velocity.

DPM
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EXHIBIT D

(2)

The UHMWPE Handbook

Ultra-High Molecular Weight Polyethylene in Total Joint Replacement

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the elemental building blocks are individual metal atoms (e.g., Co, Cr, Mo) or relatively small molecules (e.g., metal carbides or oxides). However, in a polymer, the molecular size can comprise more than a 100,000 monomer units, with molecular weights of up to millions of g/mol.

The molecular chain architecture of a polymer also imparts many unique attributes, including temperature dependence and rate dependence. Some of these unique properties are further illustrated in the specific case of UHMWPE in subsequent sections of this chapter. For further background on general polymer concepts, the reader is referred to textbooks by Rodriguez (1989) and Young (1983).

What Is Polyethylene?

Polyethylene is a polymer formed from ethylene (C_2H_4), which is a gas having a molecular weight of 28. The generic chemical formula for polyethylene is $-(C_2H_4)_n-$, where n is the degree of polymerization. A schematic of the chemical structures for ethylene and polyethylene is shown in Figure 1.4.

For UHMWPE, the molecular chain can consist of as many as 200,000 ethylene repeat units. Put another way, the molecular chain of UHMWPE contains up to 400,000 carbon atoms.

There are several kinds of polyethylene (LDPE, LLDPE, HDPE, UHMWPE), which are synthesized with different molecular weights and chain architectures. LDPE and LLDPE refer to low-density polyethylene and linear low-density polyethylene, respectively. These polyethylenes generally have branched and linear chain architectures, respectively, each with a molecular weight of typically less than 50,000 g/mol.

HDPE is a linear polymer with a molecular weight of up to 200,000 g/mol. UHMWPE, in comparison, has a viscosity average molecular weight of up to 6 million g/mol. In fact, the molecular weight is so ultra-high that it cannot be measured directly by conventional means and must instead be inferred by its intrinsic viscosity (IV).

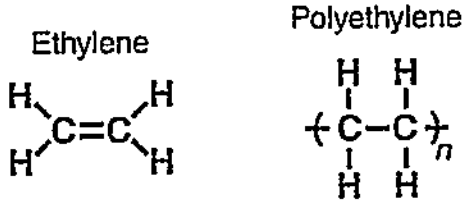

Figure 1.4
Schematic of the chemical structures of ethylene and polyethylene.

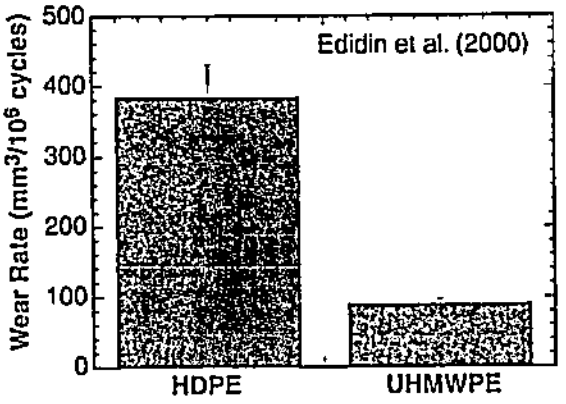

Figure 1.5
Comparison of wear rates of HDPE and UHMWPE in a multidirectional hip simulator. (From Edidin A.A., and S.M. Kurtz. 2000. The influence of mechanical behavior on the wear of four clinically relevant polymeric biomaterials in a hip simulator. *J Arthroplasty* 15:321–331.)

Crystallinity

One can visualize the molecular chain of UHMWPE as a tangled string of spaghetti, more than a kilometer long. Because the chain is not static, but imbued with internal (thermal) energy, the molecular chain can become mobile at elevated temperatures. When cooled below the melt temperature, the molecular chain of polyethylene has the tendency to rotate about the C–C bonds and create chain folds. This chain folding, in turn, enables the molecule to form local ordered, sheetlike regions known as crystalline lamellae. These lamellae are embedded within amorphous (disordered) regions and may communicate with surrounding lamellae by tie molecules. All of these morphological features of UHMWPE are shown schematically in Figure 1.6.

The degree and orientation of crystalline regions within a polyethylene depends on a variety of factors, including its molecular weight, processing conditions, and environmental conditions (such as loading), and will be discussed in later chapters.

The crystalline lamellae are microscopic and invisible to the naked eye. The lamellae diffract visible light, giving UHMWPE a white, opaque appearance at room temperature. At temperatures above the melt temperature of the lamellae, approximately 137°C, UHMWPE becomes translucent. The lamellae are on the order of 10–50 nm in thickness and 10–50 μm in length (Kurtz et al. 1999). The average spacing between lamellae is on the order of 50 nm (Bellare, Schnablegger, and Cohen 1995).

The crystalline morphology of UHMWPE can be visualized using transmission electron microscopy (TEM), which can magnify the polymer by up to

summarizes the clinical performance of UHMWPE hip implants and discusses the patterns of wear and surface damage that occur during implantation. Chapter 6 describes alternatives to conventional UHMWPE in hip replacement. Chapters 7 and 8 relate to the development and clinical performance of UHMWPE in knee replacement. Chapter 9 is devoted to clinical applications of UHMWPE in the shoulder, and Chapter 10 covers the use of UHMWPE in the spine.

The topics outlined in this *Handbook* may be used as a resource in undergraduate, as well as graduate, courses in biomaterials and orthopedic biomechanics. Students in these disciplines can learn a great deal from exposure to the historical development of total joint replacements within the context of UHMWPE. The first two main sections of this book, which cover the fundamentals of UHMWPE and clinical applications in the spine and upper and lower extremities, are intended as a resource for undergraduate instruction.

The third section of this book, which covers more specialized topics related to UHMWPE, is intended for an audience of graduate students and orthopedic researchers. Chapter 11 covers the chemistry of UHMWPE following irradiation, which leads to oxidation and crosslinking of the material. Chapter 12 describes the characterization methods for UHMWPE in the context of regulatory submissions prior to clinical trials. In Chapter 13, we review the development of the small punch test, a miniature specimen mechanical testing technique that has recently been standardized. Chapter 14 describes the micromechanical modeling of conventional and highly crosslinked UHMWPE. The final chapter in this work, Chapter 15, is a compendium of the processing, packaging, and sterilization information for highly crosslinked and thermally treated UHMWPE materials that are currently used in hip and knee arthroplasty.

Understanding basic chemical structure and morphology is an important starting point for appreciating the unique and outstanding properties of UHMWPE. The chapters that follow and describe the processing, as well as the sterilization, of UHMWPE will continue to build on the conceptual foundation established in this introduction.

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Chapter 1. Reading Comprehension Questions

1.1. Let A, B, and C be monomers. What is the molecular structure of a linear homopolymer?
- a) -A-A-B-A-A-B-A-A-B-
- b) -A-B-C-A-B-C-A-B-C-
- c) -B-C-C-C-C-C-C-C-C-
- d) -B-B-B-B-B-B-B-B-B-
- e) -C-A-A-C-A-A-C-A-A-

1.2. Which of the following polymers is NOT synthesized from ethylene?
- a) LLDPE
- b) PTFE
- c) UHMWPE
- d) HDPE
- e) LDPE

1.3. What is the major difference between HDPE from UHMWPE?
- a) Molecular weight
- b) Monomer
- c) Chemical composition
- d) Color
- e) All of the above

1.4. What are the crystals in polyethylene made up of?
- a) Folded molecular chains
- b) Calcium stearate
- c) Aluminum tetrachloride
- d) Copolymer
- e) Branched chain ends

1.5. UHMWPE exhibits which of the following transition temperatures?
- a) Glass transition
- b) Melting transition
- c) Flow transition
- d) Glass and melting transitions
- e) Glass, melting, and flow transitions

EXHIBIT E

Updated 510(k) Sterility Review Guidance K90-1; Guidance for Industry and FDA

Document issued on: August 30, 2002

This document supersedes 510(k) Sterility Review Guidance K90-1, dated November 16, 2001.

U.S. Department Of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Office of Device Evaluation

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact Timothy A. Ulatowski at (301) 443-8879 or by email tau@cdrh.fda.gov.

Additional Copies

Additional copies are available from the Internet at: http://www.fda.gov/cdrh/ode/guidance/361.pdf, or CDRH Facts-On-Demand. In order to receive this document via your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt, press 1 to order a document. Enter the document number (361) followed by the pound sign (#). Follow the remaining voice prompts to complete your request.

Updated 510(k) Sterility Review Guidance K90-1; Guidance for Industry and FDA

This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

I. Background

On November 16, 2001, the Office of Device Evaluation released updated review procedures regarding sterilization data submitted in premarket notification (510(k)) submissions as outlined in Blue Book Memorandum #K90-1, issued on February 12, 1990. The issuance of the November memorandum was deemed necessary given several significant changes that had occurred in the regulatory environment that had made aspects of the February 1990 memorandum obsolete. Specifically, these included:

1. Promulgation of the Quality System regulation (QS regulation, 21 CFR 820) in 1996;

2. Issuance of Blue Book Memorandum #K97-1 regarding changes to existing devices that can be made without submitting a new 510(k); and

3. Enactment of the Food and Drug Administration (FDA) Modernization Act of 1997 (FDAMA), which among many things, separated compliance with QS requirements from the substantial equivalence decision in most cases.

In 1997, the Center for Devices and Radiological Health (CDRH) decided that, given a manufacturer's obligation to comply with the QS requirements, the safety and effectiveness of a device manufacturer's sterilization process would best be ensured through compliance with the QS regulation rather than through 510(k) review. This decision was communicated to ODE staff and the medical device industry in Blue Book Memorandum #K97-1 entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device."[1] In this guidance, CDRH stated that manufacturers may modify existing devices in a number of ways, including labeling changes, technology or performance specification changes, and materials changes without submitting a new

[1] This guidance is available on CDRH's website at: http://www.fda.gov/cdrh/ode/510kmod.html

510(k) unless 'a change or the sum of the incremental changes exceeds the section 807.81(a)(3) threshold, "could significantly affect the safety or effectiveness of the device.'" CDRH included changes in the sterilization method as a type of change that would not normally trip the regulatory threshold for submission of a new 510(k). As stated in the guidance, changes in sterilization processes do not require 510(k) clearance, unless the changes significantly alter the properties/specifications of a device or result in a lower sterility assurance level (SAL). In instances where a manufacturer concludes that a change in sterilization method has not significantly affected device properties/specifications or resulted in a lower SAL, no 510(k) need be submitted. Rather, the appropriate documentation must be maintained at the manufacturing site in accordance with the QS regulation requirements.

The enactment of FDAMA emphasized the separation between issues of compliance with the QS regulation and determinations of substantial equivalence (SE). In a new statutory provision, the agency was instructed not to withhold a determination of the initial classification of a device because of a failure to comply with any statutory provision unrelated to the SE decision unless "there is a substantial likelihood that the failure to comply with such regulations will potentially present a serious risk to human health." This new provision, Section 513(f)(5) of the Federal Food, Drug, and Cosmetic Act, specifically includes noncompliance with good manufacturing practices (now referred to as QS requirements) as a failure that should not ordinarily delay an SE decision. These events prompted FDA to revise its procedures for the review of sterilization information in all 510(k) submissions in 1997 and to issue the November 2001 memorandum.

In recent discussions with Center staff, it was determined that additional guidance on non-traditional methods of sterilization is needed. While the agency has experience with some types of non-traditional methods of sterilization, FDA recognizes that there may be unique or novel sterilants that have not yet been submitted in a premarket notification or that have not yet been successfully implemented by device manufacturers. Given this variety in non-traditional methods, CDRH decided that additional guidance is needed to help review staff differentiate between various types of non-traditional methods of sterilization and how applications in which they are employed should be handled.

II. Methods of Sterilization

FDA considers there to be two categories of sterilization methods used to sterilize medical devices - traditional and non-traditional. Specific methods for each category are listed below.

A. Traditional Methods of Sterilization

Traditional methods of sterilization include:

- Dry heat sterilization
- Moist heat sterilization

- Ethylene Oxide (EO) with devices placed in a fixed chamber
- Radiation (gamma and electron beam)
- Liquid chemical sterilants for sterilizing single-use devices incorporating materials of animal origin

B. Non-Traditional Methods of Sterilization

In general, methods of sterilization outside the scope of specific CDRH-recognized standards are non-traditional. A new method of sterilization remains a non-traditional method unless and until: a) the specific sterilization method is incorporated into a new or existing voluntary consensus standard formally recognized by the Agency or b) CDRH evaluates the validation data for the method of sterilization as part of a quality system evaluation and finds it satisfactory for specified types of devices.

1. As of the date of this memorandum, non-traditional methods of sterilization include:

   - EO not using a fixed chamber, e.g., EO injection into a porous polymer bag. Terms used for this process include:

     - "bag method"
     - "diffusion method"
     - "sterilization pouch"
     - "injection method"
     - "validation parts 'A' and 'B'"

   Less common indications of this type of sterilization are:

     - a long gas dwell time (>8 hours) or the absence of a specified gas dwell time
     - use of EO volume (e.g., 7.2 grains) instead of concentration (e.g., 500 – 600 mg/l)
     - mention of EO (or gas) cartridge
     - use of humidichips
     - use of "100% EO in-house"

- High intensity light
- Chlorine dioxide
- Ultraviolet light
- Combined vapor and gas plasma
- Vapor systems (e.g., peroxide or peracetic acid)
- Filtration methods
- Limited use of a liquid peracetic acid system in endoscopy and with metal instruments

2. In addition to the above non-traditional sterilization methods, ODE reviewers are occasionally presented with non-traditional methods employing a unique or novel sterilant that the agency has not previously seen in a premarket submission, for which there is no related inspectional history, or for which there is little or no published literature discussing its safety and effectiveness for its intended use. Such methods include, but are not limited to, the use of microwave radiation, pulsed light, gas plasma, and sound waves. Given that the agency has had little or no experience with these methods for achieving sterilization and is concerned about a manufacturer's ability to successfully use such methods without adversely affecting the SAL, reviewers should follow the additional procedures identified below in Section IV when reviewing a 510(k) in which a sterilization method of this type is employed.

III. Review Procedures for All Sterilization Methods

Regardless of the method of sterilization, ODE scientific reviewers should gather and review the following sterilization information for all 510(k)s for devices labeled as sterile:

- The sterilization method that will be used (e.g., dry heat, moist heat,E O, radiation);
- A description of the method that will be used to validate the sterilization cycle, but not the validation data itself;
- A description of the packaging to maintain the device's sterility, not including package integrity testing data;
- If sterilization involves EO, the maximum levels of residuals of EO and ethylene chlorhydrin that remain on the device (note: the ethylene glycol

residual level was dropped from this updated guidance because the recognized standard, "ANSI/AAMI/ISO 10993-7:1995 Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide sterilization residuals," does not include measurement of ethylene glycol residuals);

- If the product is labeled "pyrogen free," a description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL);
- The SAL (e.g., 10^{-6} for all devices, except 10^{-3} for devices only contacting intact skin); and
- In the case of radiation sterilization, the radiation dose.

IV. Additional Procedures for 510(k)s Citing Non-Traditional Sterilization Methods

As delineated in Blue Book #K97-1, a manufacturer's change in the sterilization method for an existing device will generally not require the submission of a new 510(k). Similarly, a manufacturer's use of a non-traditional sterilization method should not ordinarily effect or delay a substantial equivalence determination. In assessing the impact of a sterilization method on a device, the manufacturer should ensure that the performance characteristics have not been compromised and that the SAL remains 10^{-6} (10^{-3}, as appropriate). For 510(k)s citing a non-traditional method of sterilization, scientific reviewers should notify their Branch Chief of the pending submission and proceed as described below. Situations involving non-traditional sterilization methods should be brought to the attention of the Assistant to the Director, Office of Compliance, following the procedures below, so it can be determined whether conducting an inspection of the sterilization facility is a priority.

In order to maintain consistency in our approach to non-traditional methods of sterilization, we recommend that review scientists:

1.I dentify the section in the submission related to a potential non-traditional method of sterilization;

2.Re fer a copy of the section to the Branch Chief, Infection Control Devices (INCB), Division of Dental, Infection Control and General Hospital Devices (DDIGD) for consideration; and

INCB will assess the above information related to the non-traditional sterilization method and provide feedback to the referring ODE division and to OC, as needed. If INCB determines that the method is actually a traditional method, rather than a non-traditional method, then INCB will advise the referring ODE division of this determination and no referral will be made to OC.

If, however, INCB determines that the sterilization method is a non-traditional method, INCB will advise the referring ODE division and direct the information to OC for appropriate action. OC will review the information provided and consult with INCB to decide if an inspection of the sterilization facility should be considered a priority in the postmarket period. For novel, non-traditional sterilization methods for which the Agency has had limited experience (i.e., those identified in Section II, B, 2 above), INCB, along with the ODE referring division director and the ODE Deputy Director for Science and Regulatory Policy, will work with OC management to decide if an inspection may be needed in the premarket period. Throughout all of the situations described above, INCB will provide technical consultation to ODE and OC on non-traditional sterilization methods, as each situation requires.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before a device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred by industry's attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, industry believes that there is a less burdensome way to address the issues, the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document should be followed. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

Exhibit 24

US006716234B2

(12) **United States Patent**
Grafton et al.

(10) **Patent No.: US 6,716,234 B2**
(45) **Date of Patent: Apr. 6, 2004**

(54) **HIGH STRENGTH SUTURE MATERIAL**

(75) Inventors: **R. Donald Grafton**, Naples, FL (US); **D. Lawson Lyon**, Exeter (GB); **Brian Hallet**, Taunton (GB)

(73) Assignee: **Arthrex, Inc.**, Naples, FL (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 5 days.

(21) Appl. No.: **09/950,598**

(22) Filed: **Sep. 13, 2001**

(65) **Prior Publication Data**

US 2003/0050666 A1 Mar. 13, 2003

(51) **Int. Cl.**[7] **A61L 17/04**
(52) **U.S. Cl.** **606/228**
(58) **Field of Search** 606/228

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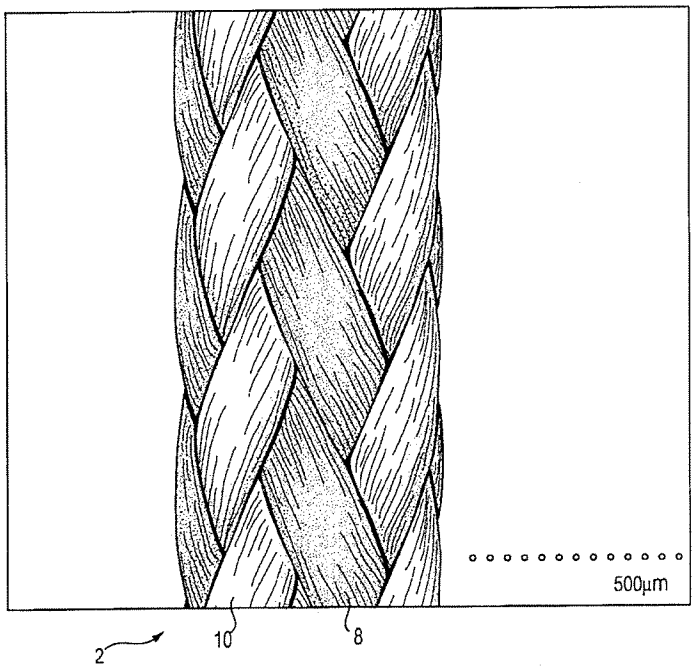
Primary Examiner—David O. Reip
(74) *Attorney, Agent, or Firm*—Dickstein Shapiro Morin & Oshinsky, LLP

(57) **ABSTRACT**

A high strength abrasion resistant surgical suture material with improved tie down characteristics. The suture features a multifilament cover formed of braided strands of ultra high molecular weight long chain polyethylene and polyester. The cover surrounds a core formed of twisted strands of ultrahigh molecular weight polyethylene. The suture, provided in a #2 size, has the strength of #5 Ethibond, is ideally suited for most orthopedic procedures, and can be attached to a suture anchor or a curved needle.

9 Claims, 2 Drawing Sheets



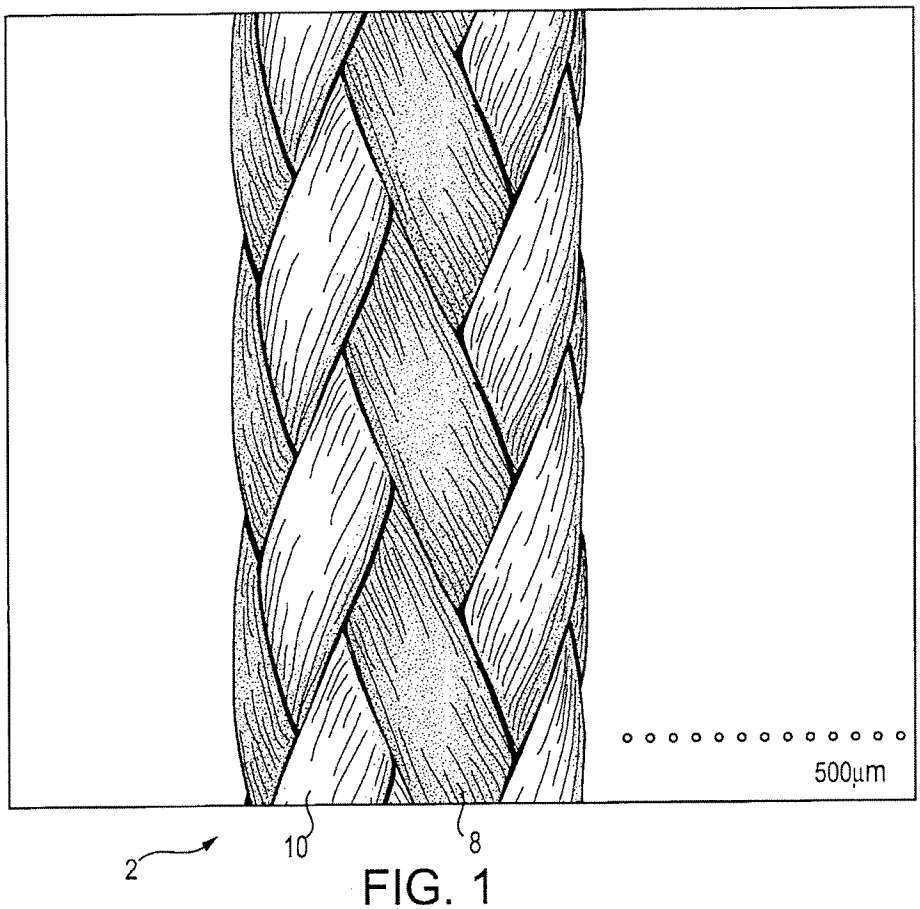


FIG. 1

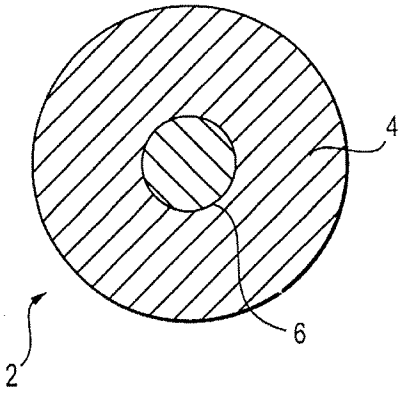


FIG. 2

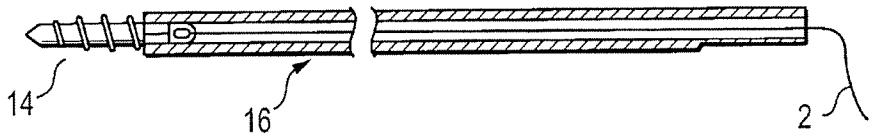


FIG. 3

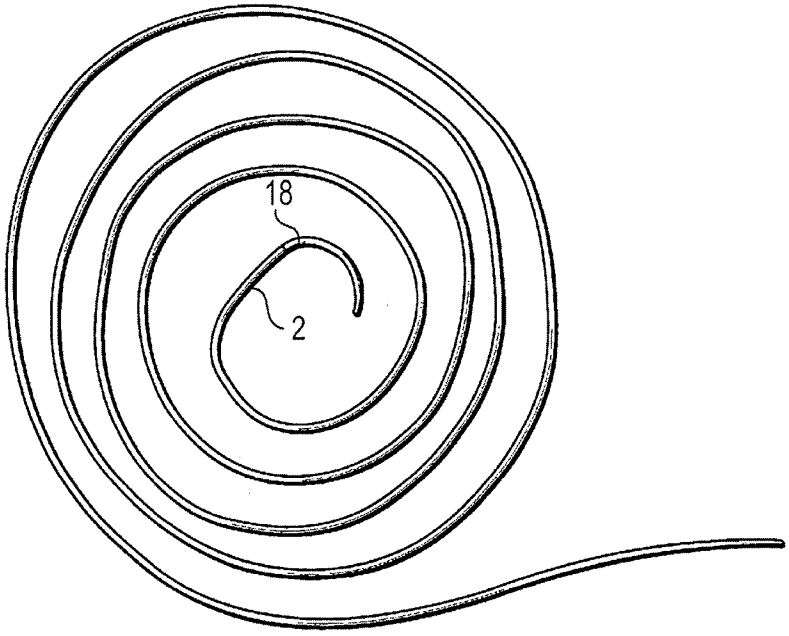


FIG. 4A

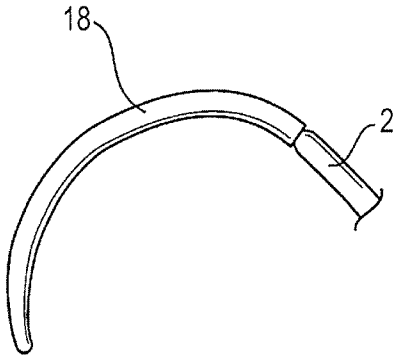


FIG. 4B

HIGH STRENGTH SUTURE MATERIAL

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to high strength surgical suture materials, and more particularly to braided suture blends of ultrahigh molecular weight polyethylene and polyester having high strength and excellent tie down characteristics.

2. Description of the Related Art

Suture strength is an important consideration in any surgical suture material. One of the strongest materials currently formed into elongated strands is an ultrahigh molecular long chain weight polyethylene, typically used for fishing line and the like, which is sold under the trade names Dyneema or Spectra. However, this material, while much stronger than ordinary surgical suture, does not have acceptable knot tie down characteristics for use in surgical applications.

SUMMARY OF THE INVENTION

The present invention advantageously provides a high strength surgical suture material with improved tie down characteristics. The suture features a braided cover made of a blend of ultrahigh molecular weight long chain polyethylene and polyester. The polyethylene provides strength. The polyester provides improved tie down properties.

The preferred suture includes a multifilament cover formed of a plurality of fibers of ultrahigh molecular weight polyethylene braided with fibers of polyester. The cover surrounds a core of twisted fibers of ultrahigh molecular weight polyethylene.

Preferably, the ultrahigh molecular weight polyethylene includes about 60% of the cover fibers, with polyester making up about 40% of the cover filaments. The core comprises about 30% of the suture, the cover making up about 70%. As an enhancement, the suture is provided with a coating on the cover, as is known in the prior art. The suture can be packaged ready for use attached to a suture anchor.

Ultrahigh molecular weight polyethylene fibers suitable for use in the present invention are marketed under the Dyneema trademark by Toyo Boseki Kabushiki Kaisha.

The suture of the present invention advantageously has the strength of Ethibond #5 suture, yet has the diameter, feel and tie ability of #2 suture. As a result, the suture of the present invention is ideal for most orthopedic procedures such as rotator cuff repair, archilles tendon repair, patellar tendon repair, ACL/PCL reconstruction, hip and shoulder reconstruction procedures, and replacement for suture in anchors.

Other features and advantages of the present invention will become apparent from the following description of the invention which refers to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWING(S)

FIG. **1** is a copy of a scanning electron micrograph of a length of suture according to the present invention.

FIG. **2** is a schematic cross section of a length of suture according to the present invention.

FIG. **3** is an illustration of the suture of the present invention attached to a suture anchor.

FIGS. **4**A and **4**B show the suture of the present invention attached to a half round, tapered needle.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring to FIG. **1**, a scanning electron micrograph of a length of suture **2** according to the present invention is shown. Suture **2** is made up of a cover **4** and a core **6** surrounded by the cover. See FIG. **2**. Strands of ultrahigh molecular weight polyethylene (UHMWPE) **8**, sold under the tradename Dyneema or Spectra, and strands of polyester **10** are braided together to form the cover **4**. The core is formed of twisted UHMWPE.

Details of the present invention will be described further below in connection with the following examples:

EXAMPLE 1

USP Size 5 (EP size 7)

Made on a 16 carrier Hobourns machine, the yarns used in the braided cover are polyester type 712 and Dyneema SK65. The cover is formed using eight carriers with one end of 190 d'tex polyester per carrier, and eight carriers with one end of 220 d'tex Dyneema per carrier. The core is formed of Dyneema using one end of 440/1/3 twisted 10 tpi "z" and 7 tpi "s" (core is not steam set). Picks per inch (PPI)=36. In forming the suture, the percent cover is 71.31, while the percent of the core is 28.69. Runnage is 1991 meters per kilo.

Of the overall suture, the polyester in the cover (8 carriers×190 d'tex=1520 d'tex) makes up 33.04% of the suture, and the Dyneema in the cover (8 carriers×220 d'tex=1760 dtex) makes up 38.76% of the suture. The Dyneema core (3 carriers×440 d'tex=1320 d'tex) is 28.69% of the suture.

EXAMPLE 2

USP Size 2

The suture is 38.09% polyester, 61.91% UHMWPE, or about 40% polyester and about 60% UHMWPE.

The examples above are for size 2 and size 5 sutures. In the making of various sizes of the inventive suture, different decitex values and different PPI settings can be used to achieve the required size and strength needed. In addition, smaller sizes may require manufacture on 12 carrier machines, for example. The very smallest sizes are made without a core. Overall, the suture may range from 5% to 90% ultrahigh molecular weight polymer (Dyneema), with the balance formed of polyester.

The suture is preferably coated with a silicon based coating to fill in voids and provide optimum run down.

The Dyneema component of the present invention provides strength, and the polyester component is provided to improve tie ability and tie down characteristics. However, it has been found that the Dyneema provides an unexpected advantage of acting as a cushion for the polyester fibers, which are relatively hard and tend to damage each other. The Dyneema prevents breakage by reducing damage to the polyester when the suture is subjected to stress.

According to an alternative embodiment of the present invention, a partially bioabsorbable suture is provided by blending a high strength material, such as UHMWPE fibers, with a bioabsorbable material, such as PLLA or one of the other polylactides, for example. Accordingly, a suture made with about 10% Dyneema blended with absorbable fibers would provide greater strength than existing bioabsorbable suture with less stretch. Over time, 90% or more of the suture would absorb, leaving only a very small remnant of the knot.

In one method of using the suture of the present invention, the suture **2** is attached to a suture anchor **14** as shown in FIG. **3** (prepackaged sterile with an inserter **16**), or is attached to a half round, tapered needle **18** as shown in FIGS. **4**A and **4**B.

Although the present invention has been described in relation to particular embodiments thereof, many other variations and modifications and other uses will become apparent to those skilled in the art. It is preferred, therefore, that the present invention be limited not by the specific disclosure herein, but only by the appended claims.

What is claimed is:

1. A suture filament suitable for use as a suture or ligature comprising:

a cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and polyester; and

a core of twisted ultrahigh molecular weight polyethylene surrounded by the cover.

2. The suture filament of claim **1**, wherein the ultrahigh molecular weight polyethylene comprises about 60% of the braided fibers.

3. The suture filament of claim **1**, wherein the polyester comprises about 40% of the braided fibers.

4. The suture filament of claim **1**, wherein the core comprises a bout 30% of the filament.

5. The suture filament of claim **1**, wherein the cover comprises about 70% of the filament.

6. The suture filament of claim **1**, further comprising a coating disposed on the cover.

7. The suture filament of claim **1**, wherein the polyester is non-absorbable.

8. A suture assembly comprising:

a suture having a multifilament cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and fibers of polyester;

a core formed of twisted fibers of ultrahigh molecular weight polyethylene; and

a suture anchor attached to the suture.

9. A suture assembly comprising:

a suture having a multifilament cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and fibers of polyester;

a core formed of twisted fibers of ultrahigh molecular weight polyethylene; and

a half round, tapered needle attached to the suture.

* * * * *

Exhibit 25

#9 Amdt D. Buyce 6/11/03

Docket No.: A8130.0013/P013
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
R. D. Grafton

Application No.: 09/950,598 Group Art Unit: 3731

Filed: September 13, 2001 Examiner: G. Phanijphand

For: HIGH STRENGTH SUTURE MATERIAL

AMENDMENT

Box Non-Fee Amendment
Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Office Action dated March 12, 2003, please cancel claim 4, amend claims 1, 3, 5-6, 8-9, and add new claim 10 in the above-identified U.S. patent application as shown in the Section marked "Amendment to the Claims".

DePuy Mitek, Inc. v. Arthrex, Inc.
C.A. No.04-12457 PBS
DMI041087

Application No.: 09/950,598 Docket No.: A8130.0013/P013

AMENDMENTS TO THE CLAIMS

1. (amended) A suture filament suitable for use as a suture or ligature comprising:

a cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and polyester; and

a core of twisted ultrahigh molecular weight polyethylene surrounded by the cover.

2. (original) The suture filament of claim 1, wherein the ultrahigh molecular weight polyethylene comprises about 60% of the braided fibers.

3. (currently amended) The suture filament of claim 1, wherein the polyester comprises about 40% of the braided ~~filaments~~ fibers.

4. (canceled)

5. (currently amended) The suture filament of claim 1, wherein the core comprises about 30% of the filament.

6. (currently amended) The suture filament of claim 1, wherein the cover comprises about 70% of the filament.

7. (original) The suture filament of claim 1, further comprising a coating disposed on the cover.

8. (currently amended) A suture assembly comprising:

a suture having a multifilament cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and fibers of polyester~~, and~~;

a core formed of twisted fibers of ultrahigh molecular weight polyethylene; and

a suture anchor attached to the suture.

9. (currently amended) A suture assembly comprising:

a suture having a multifilament cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and fibers of polyester~~, and~~;

a core formed of twisted fibers of ultrahigh molecular weight polyethylene; and

a half round, tapered needle attached to the suture.

10. (new) The suture filament of claim 1, wherein the polyester is non-absorbable.

REMARKS/ARGUMENTS

Claims 1, 3, 5, 6, 8, and 9 have been amended. Claim 4 has been canceled. Claim 10 has been added. Accordingly, claims 1-3 and 5-10 presently are pending.

Claims 1 and 4-6 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 6,045,571 to Hill et al. Claims 1 and 4-6 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,318,575 to Chesterfield et al. Claim 7 stands rejected under 35 U.S.C. § 103 as being unpatentable over Chesterfield et al. in view of U.S. Pat. No. 4,047,533 to Perciaccante et al. Applicant respectfully traverses the prior art rejections.

The present invention as recited in amended claim 1 is a suture filament suitable for use as a suture or ligature. The suture filament includes a cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and polyester, and a core of twisted ultrahigh molecular weight polyethylene surrounded by the cover.

In contrast to the present invention, Hill et al. discloses a surgical cord having a braided core. According to the disclosure of Hill et al., twisted cores are disadvantageous. Consequently, Hill et al. discloses cores formed of interlocking yarns, "as distinguished from twisted" cores. Instead of being twisted, the core yarns are "interlocked" by braiding or knitting. Thus, Hill et al. does not disclose or suggest the present invention, but rather teaches away from the present invention having a twisted core. Further, Hill et al. does not disclose suture made of ultrahigh molecular weight polyethylene. On the contrary, Hill et al. discloses polyethylene terephthalate (PET) in the molecular weight range of 30,000 to 45,000, and isotactic polypropylene homopolymer having a weight average molecular weight of from about 260,00 to about 420,000. Hill et al. does not discuss ultrahigh molecular weight polyethylene. Claim 1, and its dependent claims 2, 3 and 5-7 are submitted as being patentable over Hill et al.

Chesterfield et al. '575 discloses various surgical constructs that utilize ultrahigh molecular weight polyethylene, but does not disclose the invention recited in the claims as

presently amended. The Examiner refers to Figs. 2 and 3 and associated text from the Chesterfield et al. '575 patent, but applicant notes that these figures disclose a band 10, in contrast to the suture filament having a core and a cover as recited in claim 1 of the present application. Applicant notes further that none of the examples disclosed in the Chesterfield et al. '575 patent provides a suture having an UHMWPE core surrounded by a braided sheath or cover that includes a blend of both UHMWPE and polyester. On the contrary, the suture construction of Example 6 of Chesterfield et al. '575 has no core. The suture of Example 7 of Chesterfield et al. '575 uses a Spectra 1000 core surrounded by a hollow braided sheath made of a single type of yarn. See col. 7, line 61 to col. 8, line 5. Applicant respectfully submits that Chesterfield et al. '575 does not anticipate the present invention as recited in amended claim 1.

Claims 2 and 3 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chesterfield et al. Applicant respectfully traverses the prior art rejections.

Claims 2 and 3 of the present invention contain limitations regarding percentages of UHMWPE and polyester in the braided fibers of the suture cover. As noted above, Chesterfield et al. '575 does not disclose an example of a braided sheath that includes a blend of both UHMWPE and polyester. Consequently, it appears that the motivation for selecting a particular percentage by which the fibers are blended comes only from applicant's disclosure. Further, the Office action lacks evidence supporting the Examiner's contention regarding the knowledge in the art on varying the composition of a suture. Dependent claims 2 and 3 are submitted as being patentable over the cited references.

Claim 8 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Chesterfield in view of U.S. Pat. No. 5,720,765 to Thal. Claim 9 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Chesterfield et al. in view of U.S. Pat. No. 6,063,105 to Totakura. Applicant respectfully traverses the prior art rejections.

The present invention as recited in claim 8 is a suture assembly including a suture having a multifilament cover formed of a plurality of braided fibers of ultrahigh

molecular weight polyethylene and fibers of polyester, and a core formed of twisted fibers of ultrahigh molecular weight polyethylene. A suture anchor is attached to the suture. Claim 9 recites a suture assembly having suture with a multifilament cover formed of a plurality of braided fibers of ultrahigh molecular weight polyethylene and fibers of polyester, and a core formed of twisted fibers of ultrahigh molecular weight polyethylene. A half round, tapered needle is attached to the suture.

Chesterfield et al. '575 discloses various surgical constructs that utilize ultrahigh molecular weight polyethylene, but does not disclose the invention recited. As noted above, the Office action refers to Figs. 2 and 3 and associated text from the Chesterfield et al. '575 patent, but these figures disclose a band 10, in contrast to the suture filament having a core and a cover as recited in claims 8 and 9 of the present application. Also, none of the examples disclosed in the Chesterfield et al. '575 patent provides a suture having an UHMWPE core surrounded by a braided sheath or cover that includes a blend of both UHMWPE and polyester. On the contrary, the suture construction of Example 6 of Chesterfield et al. '575 has no core. The suture of Example 7 of Chesterfield et al. '575 uses a Spectra 1000 core surrounded by a hollow braided sheath made of a single type of yarn. See col. 7, line 61 to col. 8, line 5. Applicant respectfully submits that Chesterfield et al. '575 does not disclose the present invention as recited in claims 8 and 9.

The patents to Thal and Totakura have been cited as providing a suture anchor and a half-round, tapered needle, respectively. Neither of the patents discloses or suggests a braided suture having a blended sheath and a twisted core as recited in independent claims 8 and 9 of the present application.

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In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Dated: June 4, 2003

Respectfully submitted,

By _____

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Exhibit 26

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF MASSACHUSETTS

DEPUY MITEK, INC., a Massachusetts Corporation,

Plaintiff,

v.

ARTHREX, INC., a Delaware Corporation,

Defendant.

Civil Action

No. 04-12457 PBS

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VIDEO DEPOSITION OF STEPHEN A. SOFFEN

Washington, D.C.

Wednesday, January 4, 2006

The videotaped deposition of STEPHEN A. SOFFEN was convened on Wednesday, January 4, 2006, commencing at 9:03 a.m., at the offices of Dickstein Shapiro Morin & Oshinsky LLP, 2101 L Street, Northwest, Washington, D.C., before Cynthia R. Simmons Ott, Registered Merit Reporter, Certified Realtime Reporter, and Notary Public.

in that respect to the Hunter patent, but not applicable to the claim that Arthrex is prosecuting here because, in one case, a core is optional and, in the other, it isn't. It has to be present.

Q. But is this statement in the file history correct, that Chesterfield, et al., '575, does not disclose an example of a braided sheath that includes a blend of both ultra high molecular weight polyethylene and polyester?

A. It has to be taken in context of Claim 1. I mean, those are, this is my recollection, these are dependent claims that depend from Claim 1. Claim 1 requires a core, and the Chesterfield does not disclose an example of a suture with a core that has a braided sheath. It includes a blend of both ultra high molecular weight PE and a polyester. So you'd have to read the sentence in context of Claim 1.

Q. But on page DMI41092, you make a, make a similar statement with reference to the core versus, on 41091, the core is not mentioned?

A. We -- the reference on page six of the amendment specifically states what I just said,